ЖУРНАЛ
ОБЩЕЙ ХИМИИ

Volume 29, No. 12
December, 1959

JOURNAL OF GENERAL CHEMISTRY OF THE USSR

(ZHURNAL OBSHCHEI KHIMII)

IN ENGLISH TRANSLATION

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Volume 29, No. 12
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JOURNAL OF
GENERAL CHEMISTRY
OF THE USSR

(ZHURNAL OBSHCHEI KHIMII)

A publication of the Academy of Sciences of the USSR

IN ENGLISH TRANSLATION

Year and issue of first translation:
Vol. 19 No. 1 January 1949

	U. S. and Canada	*Foreign*
Annual Subscription	*$90.00*	*$95.00*
Annual subscription for libraries of nonprofit academic institutions	*30.00*	*35.00*
Single issue	*10.00*	*10.00*

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ÉL'FRIDA DAVYDOVNA VENUS-DANILOVA

(ON THE SEVENTIETH ANNIVERSARY OF HER BIRTH AND THE FORTY-FIFTH YEAR OF HER SCIENTIFIC AND PEDAGOGICAL ACTIVITY)

V. F. Kazimirova and L. A. Pavlova

Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12,

pp. 3857—3866, December, 1959

Original article submitted November 1, 1959

In January 1960 the great scientist and teacher, Doctor of Chemical Sciences, Él'frida Davydovna Venus-Danilova, will be 70 years of age and will have completed 45 years of scientific and pedagogical activity.

ÉL'FRIDA DAVYDOVNA VENUS-DANILOVA

In 1914 É. D. joined the physics-mathematics faculty of the St. Petersburg (Bestuzhev) Higher Women's Courses in the chemistry group, worked as an assistant, and carried out scientific work in the organic chemistry laboratory under the direction of A. E. Favorskii.

In the diploma thesis of É. D. Venus [1] on the subject, "Effect of tertiary-amylmagnesium chloride on ethyl oxalate," which was completed under the direction of V. I. Egorov and published in the Journal of the Russian Physico-Chemical Society, the reducing effect of tertiary-amylmagnesium chloride in the Grignard-Zaitsev reaction was investigated.

É. D. taught in the (Bestuzhev) Higher Women's Courses until their consolidation with the Leningrad State University in 1919. From 1922 to 1927 she gave a course in carbohydrate chemistry on the biology faculty of the university and directed laboratory work.

From 1930, as a result of the transfer of the chemical faculty of the university to the Lensovet Leningrad Institute of Chemistry and Technology, É. D. taught in the organic chemistry department of that institute. In 1932 É. D. was chosen as reader, and in 1939 professor, in the organic chemistry department. In 1930–1933 she gave a special course in organic chemistry in the Department of Artificial Fibers of the Lensovet Leningrad Institute of Technology. In 1938 É. D. defended a doctoral dissertation on the subject, "Investigation in the field of aldehydes and hydroxyaldehydes of the polymethylene series". From 1948 to 1951 she headed the Department of Organic Chemistry of the Leningrad Institute of Technology, and since 1953, without teaching duties, she has carried on scientific work and directed aspirants.

É. D. has combined scientific research and pedagogical activity with a great deal of social work. After the Great October Socialist Revolution, from 1921 to 1923, É. D. took part in the organization of the Workers' Faculty at Petrograd University and at the Politprosvetraboty Pedagogical Institute in 1925–1926; É. D. worked in elective trade-union organs for several years. É. D. was a council member of the Leningrad Division of the Mendeleev All-Union Chemical Society for several years and took an active part in its work. For more than 30 years É. D. has published a great deal of work in the Journal of General Chemistry of the USSR Academy of Sciences, and she has been a member of its editorial board since 1930.

Being a worthy representative of the scientific chemical school of Butlerov-Favorskii, É. D. has creatively developed and continued the ideas of this school by her experimental investigations in the course of 45 years. She has published more than 80 papers in domestic and foreign scientific journals.

É. D.'s scientific interests are centered on isomeric conversions of oxygen-containing compounds– aldehydes, bromo-aldehydes, hydroxyaldehydes, bromo- and hydroxy-ketones, and in recent years, glycols of the acetylene series.

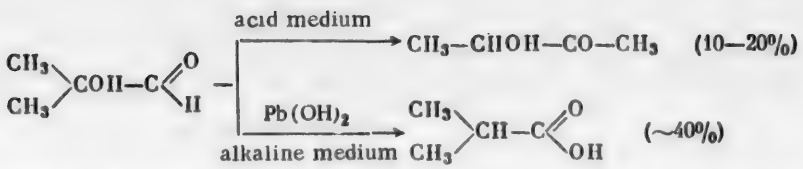
The works of A. E. Favorskii and É. D. Venus-Danilova [2] were based on oxidation-reduction reactions, which were studied in the case of isomeric conversions of the α-ketoalcohols, methylpropionylcarbinol and ethylbutyrylcarbinol, to ethylacetylcarbinol and propylpropionylcarbinol.

$$CH_3—CHOH—CO—CH_2—CH_3 \rightarrow CH_3—CO—CHOH—CH_2—CH_3$$
$$CH_3—CH_2—CHOH—CO—CH_2—CH_2—CH_3 \rightarrow CH_3—CH_2—CO—CHOH—CH_2—CH_2—CH_3$$

Acid conversion of bromoketones, which had been noticed earlier in A. E. Favorskii's laboratory, was observed here.

In a series of works from 1925 to 1929 É. D., partly together with S. N. Danilov, first observed an aldehyde-ketone rearrangement (1917) and investigated isomeric conversions of di- and trisubstituted acetaldehydes to ketones [3–8]. Together with A. I. Bol'shukhin [9, 10] she carried out the synthesis and ketonic conversion of phenylcyclohexylacetaldehyde. S. N. Danilov and É. D. Venus-Danilova showed that isomeric conversion occurs in the regeneration of trisubstituted acetaldehydes from their derivatives. The logical consequence of the study of the isomeric conversion of aldehydes was a series of works, carried out jointly with S. N. Danilov [11–13], on the isomerization of haloaldehydes and hydroxyaldehydes with an open chain, in which it was shown that the direction of the reaction depends on the conditions of the medium. On heating in alcoholic solution in the presence of a little sulfuric acid, hydroxyaldehydes are converted to hydroxyketones; in an alkaline medium in the presence of lead hydroxide or copper hydroxide, not only hydroxyketonic conversion, but also rearrangement with formation of acids occurs.

In the case of the isomerization of α-hydroxyisobutyraldehyde S. N. Danilov and É. D. Venus-Danilova [14] first carried out the acid conversion of a hydroxyaldehyde, which was predicted in 1927 by S. N. Danilov.



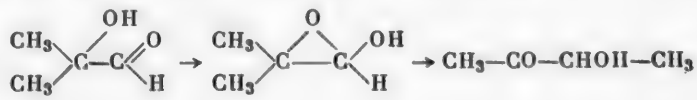
In the absence of cupric oxide and lead hydroxide an α-hydroxyaldehyde is converted by the Cannizzaro reaction to a mixture of an α-hydroxy acid and glycol. The conversion of hydroxyisobutyraldehyde to the acid is an example of intramolecular oxidation-reduction and is important in explaining the mechanism of the acid fermentation of sugars.

É. D. Venus-Danilova and V. F. Kazimirova studied isomeric conversions of the secondary α-hydroxyaldehydes: α-hydroxybutyraldehyde [15] and α-hydroxy-n-heptaldehyde [16]. It was found that secondary α-hydroxyaldehydes are more drastically isomerized in a sulfuric acid medium; instead of the expected primary α-keto alcohol(propionylcarbinol) methylacetylcarbinol and its oxidation product diacetyl were isolated, whereas butylacetylcarbinol was obtained from α-hydroxy-n-heptaldehyde.

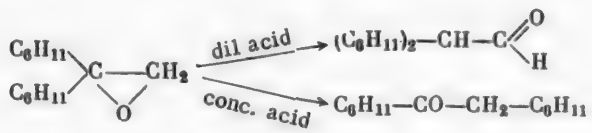
As is generally known, methylacetylcarbinol and diacetyl are formed in various biochemical processes. Much earlier, É. D. together with S. N. Danilov [17], in a study of the conversion of benzylglycolaldehyde, obtained phenylacetylcarbinol instead of the predicted primary α-keto alcohol.

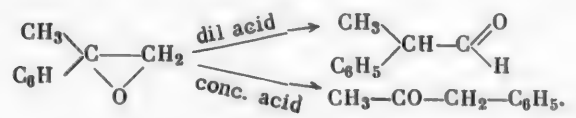
É. D. together with S. N. Danilov and P. S. Shantarovich [18] carried out the epimeric conversion of glucose to fructose under new conditions— by heating in the presence of the organic bases pyridine and quinoline. This method of investigation was used later by chemists abroad for the conversion of aldopentoses to ketopentoses. Isomeric conversion of carbonyl and hydroxycarbonyl compounds is closely connected with various biochemical processes of carbohydrates.

According to S. N. Danilov and É. D. Venus-Danilova, hydroxyaldehydes are converted to hydroxyketones in an acid medium through the intermediate formation of alcohol-oxides in conformity with the scheme proposed by A. E. Favorskii in order to explain the isomeric conversion of keto alcohols.

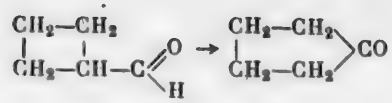


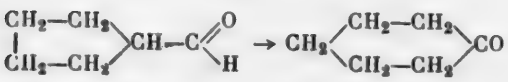
The isomerization of α-oxides is closely related to that of aldehydes and ketones. É. D. together with S. N. Danilov found that a given α-oxide may be converted either to the aldehyde or the ketone [18, 20], depending on the conditions.

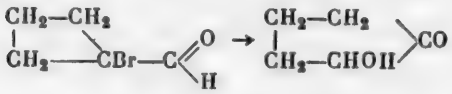




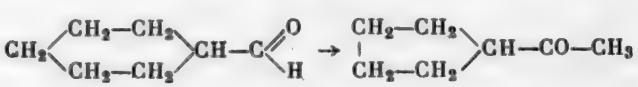
The many original works by É. D. (1932—1938) in the field of isomeric conversions of aldehydes, bromoaldehydes, and hydroxyaldehydes of the polymethylene series are of great scientific importance. In the case of cyclobutyl- [21], cyclopentyl- [22, 23], and bromocyclobutylformaldehydes É. D. found that conversion of the aldehyde to the ketone is accompanied by enlargement of the ring.



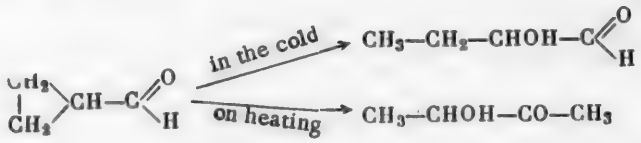




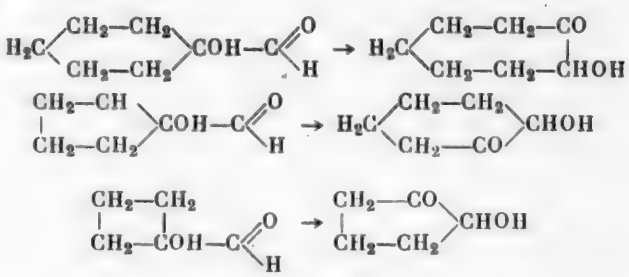
In the case of hexahydrobenzaldehyde [24] the ring becomes smaller.



The conversion of a three-membered ring (in the work of É. D. together with V. F. Kazimirova [25]) was accompanied by ring rupture and hydration; α-hydroxybutyraldehyde and its isomerization product, methylacetylcarbinol were formed.



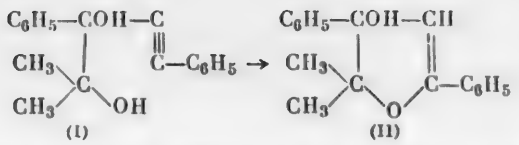
There is a large amount of experimental material [26–29] on isomeric conversions of cyclic bromo- and hydroxyaldehydes of the polymethylene series. É. D. established that cyclic hydroxyaldehydes isomerize to hydroxyketones with enlargement of the ring; moreover, they undergo acid conversion without change in the ring. Primary keto alcohols were not found.



The investigation of conversions of cyclic aldehydes, α-bromo- and α-hydroxyaldehydes, is of great interest in connection with the question of ring stability and is important in explaining conversions of organic substances in biochemical processes.

An investigation of the dehydration of secondary and tertiary alcohols of the polymethylene series, carried out by É. D. together with A. I. Bol'shukhin [30], in which the effect of certain radicals on the direction of dehydration was determined, borders on the above.

In recent years É. D. turned her attention to complex conversions of acetylenic α-glycols. These investigations were based on a work on the isomerization of an acetylenic pinacol — dimethylphenylethynylethylene glycol (I) — under the influence of sulfuric acid, carried out under the direction of A. E. Favorskii and published in 1915 [31]. Despite expectation, the indicated ditertiary α-glycol did not undergo the pinacol rearrangement, but was converted to an isomeric product giving various salts with acids and forming complex compounds. The substance obtained was assigned the structure of alcohol-oxide (II).

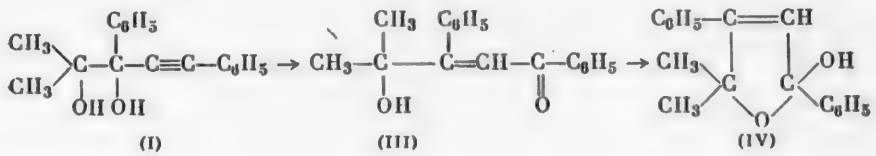


(I) (II)

The work done was of great theoretical interest, owing to the fact that for the first time a pinacol was encountered which, instead of undergoing the pinacol rearrangement, isomerized to a substance with basic properties. It was important to determine more accurately the structure of this substance and the cause of its basic properties.

In the last 15 years É. D. has devoted much initiative and labor to the study of the dependence of conversions of acetylenic α-glycols on structure and reaction conditions, and to investigation of the structure and properties of the isomeric compounds with basic properties formed from glycols.

In 1943 [32] É. D. showed that the structure of the substance obtained earlier, having basic properties, actually is not that of alcohol-oxide (II) but that of the cyclic hemiketal 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5. The formation of this product from the glycol was explained by the acetylene-allene rearrangement of glycol (I) to γ-keto alcohol (III) and cyclization of the latter to hydroxydihydrofuran (IV).



(I) (III) (IV)

This structure explains well the ability of the substance to give ketal-type ethers and to react with carbonyl-group reagents in the presence of acids, since the 2-hydroxydihydrofuran-2,5 can pass over to the isomeric ethylenic γ-keto alcohol (III).

In a work, done by É. D. together with E. P. Brichko [33], on the isomerization of dimethylphenyl-tert-butyl-ethynylethylene glycol in an acid medium, she isolated the corresponding ethylenic γ-keto alcohol and elucidated the mutual transitions of the γ-keto alcohol and the hydroxydihydrofuran in an acid medium.

Later É. D., together with E. P. Brichko, L. A. Pavlova, and V. I. Serkova [34—42] further studied the series of acetylenic α-glycols. It was shown that on treatment with sulfuric acid they may give, depending on the structure, not only substances having basic properties, but also acetylenic ketones— products of the pinacol rearrangement— and γ-keto alcohols with a double bond. The latter, however, are easily converted to dienic ketones (dehydration), or else they undergo ketonic cleavage.

Comparison of data obtained for 11 ditertiary α-glycols of the acetylene series shows how the character of the conversions depends on the structure. Thus pinacols having methyl groups on the first hydroxylated carbon atom always form compounds of the hydroxydihydrofuran series. When the methyl groups are replaced by aromatic radicals, the ability to undergo the pinacol rearrangement is more strongly developed.

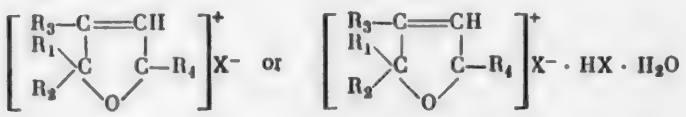
The presence of an aromatic radical on the second hydroxylated carbon atom facilitates the formation of substituted hydroxydihydrofurans.

The work of É. D. on the properties of 2-hydroxydihydrofurans-2,5 is of great interest. As a result of investigations by É. D. (together with A. Fabritsy, A. N. Orlova, et al.), this group of compounds was completely characterized.

It was established that the double bond in these substances is only slightly active; hydroxydihydrofurans are unaffected by oxidizing agents [43], and bromine adds sluggishly [32]. The most stable of the products of reaction with bromine proved to be the unsaturated bromide, which retained the characteristic hydroxydihydrofuran grouping.

In the presence of small amounts of acids, hydroxydihydrofurans pass over to isomeric ethylenic γ-keto alcohols and give carbonyl derivatives. On treatment of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 with 2,4-dinitrophenylhydrazine, not only the normal 2,4-dinitrophenylhydrazone, but also isomeric 2,4-dinitrophenylhydrazino hydrazones, were obtained, and the mutual transitions of the substances formed were elucidated [44].

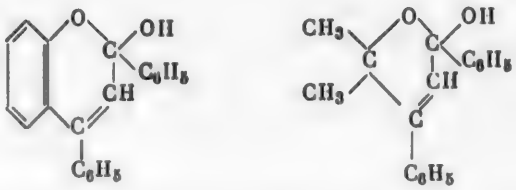
With respect to the basic properties of hydroxydihydrofurans, it was established that they are carbonium bases and that their basic properties are due to the presence of a hydroxyl group in their molecules. On treatment with acids, a reaction takes place according to the equation R—OH + HX → RX + H_2O. The salts formed have been assigned the structure:



The salts contain a conjugated carbonium cation whose stability depends on the nature of the radicals R_1, R_2, R_3, and R_4 [45, 46].

The hydroxyl group in hydroxydihydrofurans is very mobile. On hydrogenation, the hydroxyl is first replaced by hydrogen (in this case the product loses its basic properties); only then is the double bond hydrogenated [43]. Hydroxydihydrofurans easily form ketals and condense with substances containing mobile hydrogen atoms. Thus products of interaction with phenylmethylpyrazolone [45], acetic anhydride, and acetone [47] were obtained.

In their chemical properties and structure 2-hydroxydihydrofurans-2,5 are very similar to compounds of the benzopyrylium series.

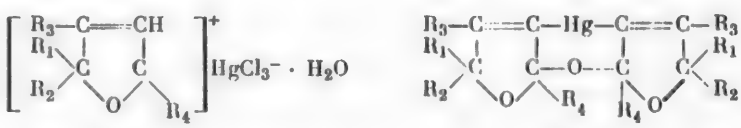


Substituted 2-hydroxydihydrofurans-2,5 may be regarded as five-membered analogs of compounds of the chromenol, flavenol, and xanthydrol series.

É. D. also investigated the conversions of ditertiary and secondary-tertiary acetylenic α-glycols under the influence of mercury salts.

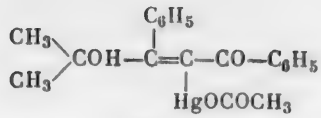
Together with V. M. Al'bitskaya [48, 49], she found that the secondary-tertiary α-glycols, diphenylphenylethynylethylene glycol and dimethylphenylethynylethylene glycol, are converted to the corresponding substituted furans on treatment with mercuric chloride. Later, with A. Fabritsy [50], she studied the effect of mercuric chloride on methylphenylphenylethynylethylene glycol, isolating the intermediate product of this reaction, 3-methyl-2,5-diphenyl-4-chloromercurifuran, as well as 3-methyl-2,5-diphenylfuran. They proposed a mechanism of conversion of secondary-tertiary α-glycols to substituted furans through addition of mercuric chloride to the triple bond with subsequent splitting out of HCl, leading to the formation of a mercurated substituted furan; the latter is decomposed by acid, being converted to a substituted furan. This mechanism explains the role of mercuric chloride in the reaction.

On treatment of ditertiary α-glycols, which can be converted to hydroxydihydrofurans in an acid medium, with mercuric chloride and bromide, the corresponding hydroxydihydrofurans were obtained, as well as their complex compounds with the mercury salt employed (V), and the organomercury compounds isolated in the form of symmetrization products (VI) [51, 52].



(V) (VI)

The use of mercuric acetate led to the formation of the mercuration product (VII) [53] corresponding to the open form.



(VII)

Diphenylmethylphenylethynylethylene glycol, which did not form a hydroxydihydrofuran, gives a dimer of undetermined structure, not containing mercury or chlorine [52], in the presence of mercuric chloride.

The isomerization of acetylenic hydroxy compounds was studied by É. D. in the case of acetylenic γ-glycols also. In work done with V. I. Ryabtseva and L. A. Grigor'eva [54] and Z. V. Printseva [55, 56], she converted substituted ditertiary and secondary-tertiary butynediols, in acid media, to tetrahydrofuranones-3 and showed that the reaction goes thru a stage of α-keto alcohols, which are formed as a result of the acetylene-allene rearrangement of the glycols.

The main results of the works on isomerization of aceylenic glycols may be formulated in the following theses. Under the influence of acids and mercury salts, acetylenic glycols are isomerized in several directions, which are determined by the structure of the glycol and the reaction conditions. Acetylenic glycols may be converted to compounds of the furan series, secondary-tertiary α-glycols giving substituted furans, ditertiary α-glycols giving hydroxydihydrofurans, and acetylenic γ-glycols giving furanones-3. Hydroxydihydrofurans are carbonium bases and are similar in the chemical respect to compounds of the benzopyranol and triarylcarbinol series.

É. D.'s main characteristics are her exceptional industry, love for science, creative enthusiasm, and consideration and sympathy for people. She is a brilliant experimenter and an excellent teacher. During her scientific and pedagogical career, É. D. has trained a great number of chemists, who are working in industrial enterprises, higher training institutes, and scientific research institutes in the USSR and foreign countries. The Soviet Government and the Communist Party of the Soviet Union highly esteemed the scientific services of É. D. Venus-Danilova and awarded her the Order of Lenin and several medals.

LITERATURE CITED

[1] É. D. Venus, Zhur. Russ. Fiz.-Khim. Obshchestva 46, 1333 (1914).

[2] A. E. Favorskii and É. D. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 60, 399, 409 (1928).

[3] S. Danilov and É. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 57, 347 (1925); Ber. 59, 962 (1926).

[4] S. Danilov and É. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 57, 428 (1925); Ber. 59, 1032(1926).

[5] É. D. Venus-Danilova and S. N. Danilov, Zhur. Russ. Fiz.-Khim. Obshchestva 58 (prot. 14, 126) (1926).

[6] S. N. Danilov and É. D. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 58, 957 (1926); Ber. 59, 377 (1926).

[7] É. D. Venus-Danilova and S. N. Danilov, Zhur. Russ. Fiz.-Khim. Obshchestva 59, 22 (1927); Ber. 60, 1050 (1927).

[8] É. D. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 61, 54 (1929); Ber. 61, 1954(1929).

[9] É. D. Venus-Danilova and A. I. Bol'shukhin, Zhur. Obshchei Khim. 7, 2823 (1937).

[10] É. D. Venus-Danilova and A. I. Bol'shukhin, Zhur. Obshchei Khim. 9, 976 (1939).

[11] S. N. Danilov and É. D. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 61, 1661 (1929); Ber 62, 2653 (1929).

[12] S. N. Danilov and É. D. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 62, 1697 (1930); Ber. 63, 2765 (1930).

[13] É. D. Venus-Danilova and S. N. Danilov, Zhur. Obshchei Khim. 2, 645 (1932).

[14] S. N. Danilov and É. D. Venus-Danilova, Zhur. Obshchei Khim. 3, 559 (1933).

[15] É. D. Venus-Danilova and V. F. Kazimirova, Zhur. Obshchei Khim. 16, 2099 (1946).

[16] É. D. Venus-Danilova and V. F. Kazimirova, Zhur. Obshchei Khim. 18, 1816 (1948).

[17] S. N. Danilov and É. D. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 62, 1697 (1930).

[18] S. N. Danilov, É. D. Venus-Danilova, and P. S. Shantarovich, Zhur. Russ. Fiz.-Khim. Obshchestva 62, 1377 (1927).

[19] S. N. Danilov and É. D. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 59, 197 (1927); Ber 60, 1059 (1927).

[20] É. D. Venus-Danilova, Zhur. Russ. Fiz.-Khim. Obshchestva 61, 1479 (1929).

[21] É. D. Venus-Danilova, Zhur. Obshchei Khim. 8, 1179 (1938).

[22] É. D. Venus-Danilova, Zhur. Obshchei Khim. 6, 917 (1936).

[23] É. D. Venus-Danilova, Zhur Obshchei Khim. 6, 1757 (1936).

[24] É. D. Venus-Danilova, Zhur. Obshchei Khim. 6, 697 (1936).

[25] É. D. Venus-Danilova and V. F. Kazimirova, Zhur. Obshchei Khim. 8, 1438 (1938).

[26] É. D. Venus-Danilova, Zhur. Obshchei Khim. 6, 1784 (1936).

[27] É. D. Venus-Danilova, Zhur. Obshchei Khim. 6, 1863 (1936).

[28] É. D. Venus-Danilova and V. F. Kazimirova, Zhur. Obshchei Khim. 7, 2639 (1937).

[29] É. D. Venus-Danilova, Zhur. Obshchei Khim. 8, 477 (1938).

[30] É. D. Venus-Danilova and A. I. Bol'shukhin, Zhur. Obshchei Khim. 12, 73 (1942).

[31] A. E. Favorskii and É. D. Venus, Zhur. Russ. Fiz.-Khim. Obshchestva 47, 133 (1915).

[32] É. D. Venus-Danilova, Zhur. Obshchei Khim. 13, 93 (1943).

[33] É. D. Venus-Danilova and E. P. Brichko, Zhur. Obshchei Khim. 17, 1549 (1947).

[34] É. D. Venus-Danilova and E. P. Brichko, Zhur. Obshchei Khim. 17, 1849 (1947).

[35] É. D. Venus-Danilova, E. P. Brichko, and L. A. Pavlova, Zhur. Obshchei Khim 19, 951 (1949).•

[36] É. D. Venus-Danilova and L. A. Pavlova, Zhur. Obshchei Khim. 19, 1755 (1949). •

[37] É. D. Venus-Danilova and L. A. Pavlova, Zhur. Obshchei Khim. 20, 82 (1950). •

[38] É. D. Venus-Danilova, V. I. Serkova, and L. A. Pavlova, Zhur. Obshchei Khim 21, 2211 (1951). •

[39] É. D. Venus-Danilova and V. I. Serkova, Zhur. Obshchei Khim. 22, 1563 (1952). •

[40] É. D. Venus-Danilova and V. I. Serkova, Zhur. Obshchei Khim. 24, 998 (1954). •

[41] É. D. Venus-Danilova, V. I. Serkova and A. V. El'tsov, Zhur. Obshchei Khim. 27, 334 (1957). •

[42] É. D. Venus-Danilova and V. I. Serkova, Zhur. Obshchei Khim. 28, 1477 (1958). •

[43] É. D. Venus-Danilova and A. Orlova, Zhur. Obshchei Khim. 22, 333 (1952). •

[44] É. D. Venus-Danilova, L. A. Pavlova and A. Fabritsy, Zhur. Obshchei Khim. 27, 2423 (1957). •

[45] É. D. Venus-Danilova and A. Fabritsy, Zhur. Obshchei Khim. 26, 884 (1956). •

[46] É. D. Venus-Danilova, A. Fabritsy, and A. N. Orlova, Zhur. Obshchei Khim. 26, 1160 (1956). •

[47] É. D. Venus-Danilova, L. A. Pavlova, and A. Fabritsy, Zhur. Obshchei Khim. 28, 658 (1958). •

•Original Russian pagination. See C. B. translation.

[48] É. D. Venus-Danilova and V. M. Al'bitskaya, Zhur. Obshchei Khim. 22, 816 (1952). •

[49] É. D. Venus-Danilova and V. M. Al'bitskaya, Zhur. Obshchei Khim. 22, 1568 (1952). •

[50] É. D. Venus-Danilova and A. Fabritsy, Zhur. Obschei Khim. 28, 3227 (1958). •

[51] É. D. Venus-Danilova and A. Fabritsy, Zhur. Obshchei Khim. 26, 1609 (1956). •

[52] É. D. Venus-Danilova and A. Fabritsy, Zhur. Obshchei Khim. 26, 2458 (1956). •

[53] É. D. Venus-Danilova and A. Fabritsy, Zhur. Obshchei Khim. 26, 1901 (1956). •

[54] É. D. Venus-Danilova, V. I. Ryabtseva, and L. A. Grigor'eva, Zhur. Obshchei Khim. 24, 1380 (1954). •

[55] É. D. Venus-Danilova and Z. V. Printseva, Zhur. Obshchei Khim. 25, 1516 (1955). •

[56] É. D. Venus-Danilova and Z. V. Printseva, Zhur. Obshchei Khim. 26, 2170 (1956). •

•Original Russian pagination. See C. B. translation.

2,5-DIMETHYLFURANIDONE-3 IN THE SYNTHESIS OF 2,5-DIMETHYL-3-ALKYL- AND 2,5-DIMETHYL-3-ARYLFURANIDINES

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12,

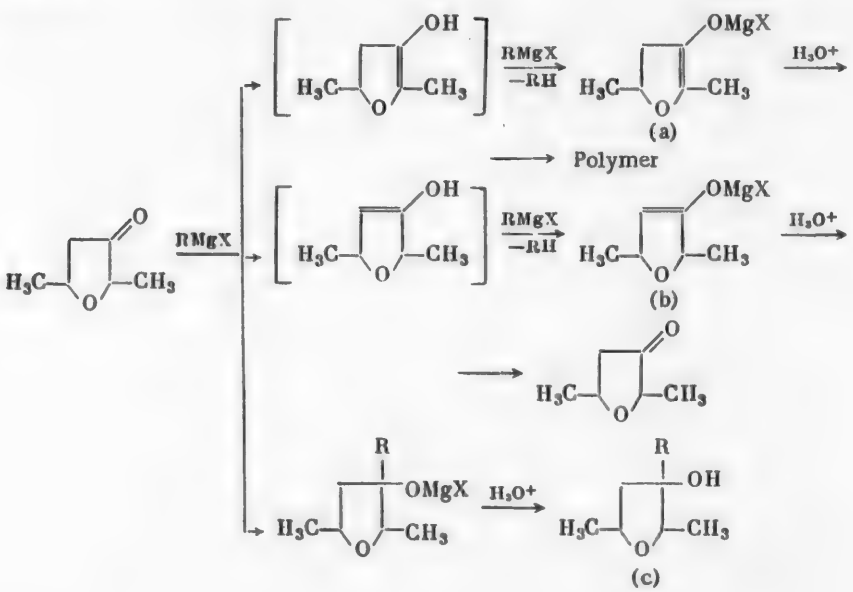
pp. 3867-3872, December, 1959

Original article submitted November 24, 1958

In the preceding works [1, 2] we showed that 2,5-dimethylfuranidone-3, which is easily prepared by isomerizing hexyne-3-diol-2,5 in the presence of mercuric sulfate [3], may serve as a convenient substance for the synthesis of 2,5-dimethyl-3-alkylfuranidines having alkyl radicals of normal structure (CH_3, C_2H_5, C_3H_7, C_4H_9) in position 3.

In the present work we used this method for the synthesis of 2,5-dimethyl-3-alkylfuranidines with more complex and branched aliphatic radicals; cases were observed in which the course of the reaction was anomalous. Thus in the interaction of 2,5-dimethylfuranidone-3 with cyclohexylmagnesium chloride the corresponding tertiary alcohol was not obtained; the bulk of the reaction product was a polymer of indefinite composition, only 10% of the original ketone being recovered, while up to 70% of cyclohexane was obtained.

In the reaction of 2,5-dimethylfuranidone-3 with isopropylmagnesium bromide, we obtained 2,5-dimethyl-3-isopropyl-3-hydroxyfuranidine in 10% yield, and unchanged 2,5-dimethylfuranidone-3. Such results apparently are due to the fact that 2,5-dimethylfuranidone-3 reacts with secondary alkylmagnesium halides simultaneously in the keto and enol forms:



Owing to the dual reactivity manifested by 2,5-dimethylfuranidone-3, three different alkoxides— (a), (b), and (c) — are formed in the reaction; on decomposition of the reaction mixture with acidified water they give different reaction products. Thus in the case of enolization with participation of a hydrogen atom from position 2 of the ring, which should lead to formation of a cyclic vinyl ether— scheme (a) —the latter is hydrolyzed and the hydrolysis product polymerized; in the case of enolization with participation of hydrogen from position 4 of the ring—scheme (b)— the original 2,5-dimethylfuranidone-3 is regenerated on decomposition of the alkoxide; finally, in the case of a reaction in the keto form— scheme (c)— the corresponding tertiary alcohol, the 2,5-dimethy-3-alkyl-3-hydroxyfuranidine, is obtained.

Thus the enolization of 2,5-dimethylfuranidone-3, caused by secondary alkylmagnesium halides, is much more pronounced than that of carbocyclic ketones in analogous cases [4].

As regards alkylmagnesium halides obtained from primary halides with branched radicals, their reaction with 2,5-dimethylfuranidone-3 leads to the corresponding 2,5-dimethyl-3-alkyl-3-hydroxyfuranidines, the yield of the corresponding hydroxyfuranidine rising with increase of the distance from the branching point of the chain to the carbon atom bound to halogen. Thus in the interaction of 2,5-dimethylfuranidone-3 with isobutylmagnesium bromide, 2,5-dimethyl-3-isobutyl-3-hydroxyfuranidine was obtained in 28% yield, while in the reaction with isoamylmagnesium bromide the yield of 2,5-dimethyl-3-isoamyl-3-hydroxyfuranidine reached 65%; we obtained 2,5-dimethyl-3-n-amyl-3-hydroxyfuranidine in the same yield (66%). On bringing arylmagnesium halides into reaction with 2,5-dimethylfuranidone-3, we obtained 2,5-dimethyl-3-aryl-3-hydroxyfuranidines.

The dehydration of 2,5-dimethyl-3-alkyl-3-hydroxyfuranidines by p-toluenesulfonic acid takes place with the formation of mixtures of isomeric dihydrofurans, together with products of their further conversion. We isolated such dihydrofuran mixtures in the form of fractions with wide boiling ranges from the dehydration product by fractional distillation, and then subjected them to catalytic dehydrogenation.

The dehydration of 2,5-dimethyl-3-aryl-3-hydroxyfuranidines goes more simply and smoothly, since, of the two theoretically possible isomeric types of dihydrofurans— 2,5-dimethyl-3-aryl-$\Delta^{3,4}$- and 2,5-dimethyl-3-aryl-$\Delta^{2,3}$-dihydrofurans— only the first is obtained in practice; when the dehydration product was shaken with a saturated solution of 2,4-dinitrophenylhydrazine in 2 N hydrochloric acid, only a slight turbidity was obtained in the solution. The absence of the second isomer in the dehydration product apparently is due to its lability under the more severe conditions which we used in the dehydration reaction.

The hydrogenation of the corresponding 2,5-dimethyl-3-aryldihydrofurans under pressure in the cold in the presence of platinum also goes more smoothly and with better yields than that of 2,5-dimethyl-3-alkyldihydrofurans.

As regards 2,5-dimethyl-3-cyclohexylfuranidine, we prepared it by catalytically hydrogenating 2,5-dimethyl-3-phenyl-3-hydroxyfuranidine at 165° in a circulating system at atmospheric pressure in the presence of nickel on aluminum oxide; hydrogenation at 85° led to 2,5-dimethyl-3-phenylfuranidine, whose constants differed somewhat from those of a sample which we prepared by hydrogenating 2,5-dimethyl-3-phenyldihydrofuran in the cold in the presence of a platinum catalyst. This is undoubtedly due to the fact that 2,5-dimethyl-3-phenylfuranidine can exist in four stereoisomeric forms, the relative amounts of stereoisomers in the mixture being determined, as usual, by the nature of the catalyst and the hydrogenation conditions.

Constants and yields of the 2,5-dimethyl-3-alkyl- and 2,5-dimethyl-3-arylfuranidines obtained by us are given in the table.

EXPERIMENTAL

I. Synthesis of 2,5-dimethyl-3-alkyl (or aryl)-3-hydroxyfuranidines

a) To an ethereal solution of the alkylmagnesium bromide, prepared from 1.3 moles of magnesium and 1.3 moles of the alkyl bromide in 300 ml of absolute ether, in a flask provided with an efficient stirrer, dropping funnel, and reflux condenser with a drying tube, 1 mole of 2,5-dimethylfuranidone-3 in 100 ml of absolute ether was added dropwise, the flask being cooled to 0°; stirring was then continued for 1 hour more. After decomposition of the reaction mass with a saturated solution of ammonium acetate in 2 N acetic acid, the ether layer was separated and the water layer extracted with ether. The ethereal extracts were dried with potash, the ether driven off, and the residue fractionated in vacuo.

2,5-Dimethyl-3-isopropyl-3-hydroxyfuranidine. From 31.2 g of magnesium, 159.9 g of isopropyl bromide, and 114 g of 2,5-dimethylfuranidone-3 in 400 ml of absolute ether, 15.8 g (10%) was obtained.

B.p. 190–191° (767 mm), n_D^{20} 1.4500, d_4^{20} 0.9490, MR_D 44.80; calcd. 44.85

Found %: C 68.07, 68.01; H 11.44, 11.42. $C_9H_{18}O_2$. Calculated %: 68.31; H 11.47.

2,5-Dimethyl-3-isobutyl-3-hydroxyfuranidine. From 31.2 g of magnesium, 178.1 g of isobutyl bromide, and 114 g of 2,5-dimethylfuranidone-3 in 400 ml of absolute ether, 48.2 g (28%) was obtained.

B.p. 204–205° (737 mm), 79–80° (5 mm), n_D^{20} 1.4502, d_4^{20} 0.9435, MR_D 49.06 calcd. 49.35.

Found %: C 69.41, 69.37; H 11.68, 11.67. $C_{10}H_{20}O_2$. Calculated %: C 69.73; H 11.70.

2,5-Dimethyl-3-amyl-3-hydroxyfuranidine. From 31.2 g of magnesium, 196.3 g of amyl bromide, and 114 g of 2,5-dimethylfuranidone-3 in 400 ml of absolute ether, 122.7 g (66%) was obtained.

B.p. 222–223° (735 mm), 99–100° (5 mm), n_D^{20} 1.4526, d_4^{20} 0.9317, MR_D 53.76; calcd. 53.96.

Found %: C 70.56, 70.56; H 11.80, 11.78. $C_{11}H_{22}O_2$. Calculated %: C 70.91; H 11.87.

2,5-Dimethyl-3-isoamyl-3-hydroxyfuranidine. From 31.2 g of magnesium, 196.3 g of isoamyl bromide, and 114 g of 2,5-dimethylfuranidone-3 in 400 ml of absolute ether, 120.2 g (65%) was obtained.

B.p. 217–218° (740 mm), 95.5–96° (6 mm), n_D^{20} 1.4512, d_4^{20} 0.9349, MR_D 53.66; calcd. 53.96.

Found %: C 70.57, 70.50; H 11.79, 11.71. $C_{11}H_{22}O_2$. Calculated %: C 70.81; H 11.87.

b) As described in "a," 0.5 mole of magnesium, 0.5 mole of the aryl bromide, and 0.5 mole of 2,5-dimethylfuranidone-3 were brought into reaction in 200 ml of absolute ether. The alkoxide was decomposed with 3 N acetic acid, the ether layer separated, and the water layer extracted with ether. The ethereal extracts were dried with magnesium sulfate, the ether driven off, and the residue fractionated in vacuo.

2,5-Dimethyl-3-phenyl-3-hydroxyfuranidine. From 12 g of magnesium, 78.5 g of bromobenzene, and 57 g of 2,5-dimethylfuranidone-3 in 500 ml of absolute ether, 51 g (63%) was obtained.

B.p. 126–127° (8 mm), m.p. 57.5–58° (from petroleum ether).
Found %: C 75.10, 75.08; H 8.51, 8.38. $C_{12}H_{16}O_2$. Calculated %: C 74.96; H 8.39.
Literature data [5]: b.p. 138–140° (16 mm), d_4^{20} 1.0827, n_D^{20} 1.5310.

2,5-Dimethyl-3-benzyl-3-hydroxyfuranidine. From 12 g of magnesium, 63.3 g of benzyl chloride, and 57 g of 2,5-dimethylfuranidone-3 in 500 ml of absolute ether, 45 g (43.5%) was obtained.

B.p. 275–276° (735 mm), 148–149° (10 mm), n_D^{20} 1.5252, d_4^{20} 1.0558, MR_D 59.89; calcd. 59.59.

Found %: C 75.60, 75.67; H 8.92, 8.84. $C_{13}H_{18}O_2$. Calculated %: C 75.69; H 8.79.
Literature data [5]: b.p. 146–147° (15 mm), n_D^{20} 1.5251, d_D^{20} 1.0598.

2,5-Dimethyl-3-p-tolyl-3-hydroxyfuranidine. From 12 g of magnesium, 85.5 g of p-bromotoluene, and 57 g of 2,4-dimethylfuranidone-3 in 500 ml of absolute ether, 42.5 g (41%) was obtained.

M.p. 69–70° (from petroleum ether).
Found %: C 75.48, 75.46; H 8.83, 8.80. $C_{13}H_{18}O_2$. Calculated %: C 75.69; H. 8.79.
Literature data [5]: b.p. 149–150° (15 mm), d_4^{15} 1.0456, n_D^{15} 1.5288.

II. Dehydration of 2,5-Dimethyl-3-alkyl (or aryl)-3-hydroxyfuranidines

a) 0.05–0.1 mole of the 2,5-dimethyl-3-alkyl-3-hydroxyfuranidine was boiled for 2–2.5 hours with 0.5–1 g of p-toluenesulfonic acid, and the dehydration product slowly distilled off. The product in the distallate was separated from the water, dried with magnesium sulfate, and fractionated in vacuo.

Thus, broad fractions, containing isomers of the following 2,5-dimethyl-3-alkyldihydrofurans, were isolated: 2,5-dimethyl-3-isobutyldihydrofuran (53%); b.p. 50–70° (10 mm); 2,5-dimethyl-3-amyldihydrofuran (60%), b.p. 60–80° (8 mm); 2,5-dimethyl-3-isoamyldihydrofuran (69%), b.p. 80–100° (20 mm).

TABLE

Constants of 2,5-Dimethyl-3-alkyl- and 2,5-dimethyl-3-arylfuranidines

Compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		Yield, reckoned on dihydrofuran (in %)	Total amount obtained (in g)	% C		% H	
				found	calculated			found	calculated	found	calculated
2,5-Dimethyl-3-isobutylfuranidine	69—70 (20)	1.4390	0.8559	48.02	47.82	46.5	22	76.58, 76.50	76.84	12.80, 12.77	12.77
2,5-Dimethyl-3-isoamylfuranidine	195—196 (750)	1.4466	0.8620	52.74	52.44	50	30.2	77.81, 77.97	77.80	13.16, 13.20	12.98
2,5-Dimethyl-3-n-amylfuranidine	197—198 (750)	1.4440	0.8607	52.50	52.44	47	33	77.78, 77.68	77.80	13.05, 13.07	12.98
2,5-Dimethyl-3-cyclohexylfuranidine*	104—105 (14)	1.4902	0.9464	55.72	55.47	12	10	79.35, 79.30	79.04	12.08, 12.05	12.16
2,5-Dimethyl-3-phenylfuranidine	101—102 (10)	1.5225	0.9859	53.94	54.23	75.5	39	81.86, 81.90	81.77	8.82, 9.00	9.15
2,5-Dimethyl-3-phenylfuranidine*	105—106 (11)	1.5308	0.9897	54.44	54.23	8.5	16	81.84, 81.75	81.77	8.87, 8.94	9.15
2,5-Dimethyl-3-benzylfuranidine	121—122 (10)	1.5128	0.9636	58.73	58.92	79	38.5	82.01, 81.97	82.06	9.50, 9.53	9.53
2,5-Dimethyl-3-p-tolylfuranidine	115—116 (10)	1.5140	0.9706	59.02	58.92	76.5	21	82.10, 82.18	82.06	9.49, 9.43	9.53

* Obtained through the catalytic hydrogenation of 2,5-dimethyl-3-phenyl-3-hydroxyfuranidine in the presence of nickel on aluminum oxide.

b) 0.05—0.1 mole of the 2,5-dimethyl-3-aryl-3-hydroxyfuranidine was heated for 1.5—2 hours with 0.5—1 g of p-toluenesulfonic acid at 150—160°. After cooling, the reaction product was extracted with ether and the extract washed with water and soda, and dried with magnesium sulfate. The ether was driven off and the residue fractionated in vacuo.

2,5-Dimethyl-3-phenyldihydrofuran. /A 19.2 g quantity of 2,5-dimethyl-3-phenyl-3-hydroxyfuranidine and 1 g of p-toluenesulfonic acid were used. Fifteen g (86%) was obtained.

B.p. 112.5—113.5° (12 mm), n_D^{20} 1.5468, d_4^{20} 1.0149, MR_D 54.43; calcd. 53.75.
Found %: C 82.60, 82.78; H 8.32, 8.39. $C_{12}H_{14}O$. Calculated %: C 82.72; H 8.29.

2,5-Dimethyl-3-benzyldihydrofuran. A 20.6 g quantity of 2,5-dimethyl-3-benzyl-3-hydroxyfuranidine and 1 g of p-toluenesulfonic acid were used. There was obtained 11.5 g (61%).

B.p. 119.5—120.5° (10 mm), n_D^{20} 1.5285, d_4^{20} 0.9831, MR_D 59.01; calcd. 58.19.
Found %: C 82.90, 82.95; H 8.56, 8.50. $C_{13}H_{16}O$. Calculated %: C 82.93; H 8.56.

2,5-Dimethyl-3-p-tolyldihydrofuran. A 10.3 g quantity of 2,5-dimethyl-3-p-tolyl-3-hydroxyfuranidine and 0.5 g of p-toluenesulfonic acid were used. There was obtained 7.02 g (74.5%).

B.p. 122.5—123.5° (10 mm), n_D^{20} 1.5370, d_4^{20} 0.9918, MR_D 58.68; calcd. 58.19.
Found %: C 83.07, 83.11; H 8.53, 8.54. $C_{13}H_{16}O$. Calculated %: C 82.99; H 8.56.

III. Preparation of 2,5-Dimethyl-3-alkyl (or aryl)-furanidines

a) From 0.15 to 0.25 mole of the 2,5-dimethyl-3-alkyl (or aryl)-dihydrofuran, either without solvent (in the case of a 2,5-dimethyl-3-alkyldihydrofuran) or in 25 ml of anhydrous alcohol (in the case of a 2,5-dimethyl-3-aryldihydrofuran), was hydrogenated in an autoclave, in the presence of 0.4—0.5 g of Adams platinum catalyst, [6], at 60—70 atm. After absorption of 80% of the calculated quantity of hydrogen, the hydrogenation product was treated with sodium (the solvent being distilled off first if one was used), distilled from the precipitate in vacuo, and the distillate treated with a 30% solution of bromine in chloroform at -15° until it acquired a stable yellow hue. After standing for a day, the substance was distilled from the bromides in vacuo, treated again with sodium, and distilled from the precipitate in vacuo, and finally fractionated in a column (36 theoretical plates).

b) On hydrogenating 38.4 g of fused 2,5-dimethyl-3-phenyl-3-hydroxyfuranidine in a circulating system with a space velocity of 0.05 hr^{-1} in the presence of nickel on aluminum oxide at 160—165°, 5 g (12%) of 2,5-dimethyl-3-cyclohexylfuranidine was obtained.

On hydrogenation at 80—85°, with a space velocity of 0.15 hr^{-1}, 3 g (8.5%) of 2,5-dimethyl-3-phenylfuranidine was obtained.

The constants of these furanidine homologs also are given in the table.

SUMMARY

1. The method of synthesis of 2,5-dimethyl-3-alkyl- and 2,5-dimethyl-3-arylfuranidines described by us is general for the preparation of furanidine homologs of this type.

2. 2,5-Dimethylfuranidone-3 reacts with secondary alkylmagnesium halides both in the keto and enol forms.

3. The hydrogenation of 2,5-dimethyl-3-phenyl-3-hydroxyfuranidine in a circulating system in the presence of nickel on aluminum oxide at 85°, leads to 2,5-dimethyl-3-phenylfuranidine, and at 165°, to 2,5-dimethyl-3-cyclohexylfuranidine.

LITERATURE CITED

[1] Yu. K. Yur'ev, E. G. Rozantsev and S. N. Godovikova, Zhur. Obshchei Khim. 28, 1168 (1958).*

[2] Yu. K. Yur'ev, E. G. Rozantsev and B. G. Gribov, Khim. Nauka i Prom. 3, 830 (1958).

[3] Zh. I. Iotsich, Zhur. Russ. Fiz.-Khim. Obshchestva 34, 242 (1902).

[4] V. Grignard and H. Blanchon, Roczn. Chem. 9, 547 (1939).

[5] G. Dupont, Ann. Chim. 8 [30], 500 (1913).

[6] Sintezy Org. Prep. 1, 357 (1949).

* Original Russian pagination. See C. B. translation

TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

XXVI. RELATIVE ACTIVITY OF TETRAACYLOXYSILANES AND ACYLOXYTRICHLOROSILANES IN THE REACTION OF ACYLATION OF BENZENE AND THIOPHENE

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp 3873–3880, December, 1959

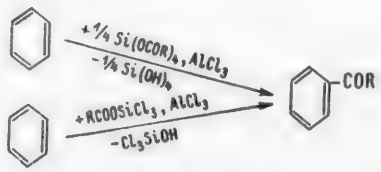
Original article submitted November 24, 1958

In the preceding works, we found that monobasic organic acids, both of the aromatic [1] and aliphatic series [2], quantitatively form the corresponding acyloxytrichlorosilanes on treatment with an excess of silicon tetrachloride. Since benzoxytrichlorosilane displayed high acylating power [3], we devoted the present work to a comparative study of the acylation of benzene and thiophene by acyloxytrichlorosilanes and tetraacyloxysilanes with identical acyloxy groups.

According to the data of one of us and co-workers, tetraacyloxysilanes are extremely convenient for the acylation of benzene [4], thiophene [5–7], and selenophene nuclei [8], since they permit high yields of ketones and keto acids in these series.

According to literature data, aromatic and heterocyclic acid chlorides, for the most part, have been used for the preparation of aromatic ketones. Thus on acylation of benzene with toluyl, chlorobenzoyl, nitrobenzoyl, α-naphthoyl, and furoyl chlorides, the corresponding ketones were obtained in 68–93% yields [9–17]; α-naphthyl thienyl ketone was obtained in 59–75% yield on acylation of naphthalene with thenoyl chloride [18]. On treatment of thiophene with furoyl chloride in the presence of stannic chloride, Gilman and co-workers [19] obtained 2-furyl 2-thienyl ketone in 66% yield. By acylating thiophene with thenoyl chloride, Blicke and Anderson [20] obtained di-2-thienyl ketone in 77% yield.

In the present work, we acylated benzene with acyloxytrichlorosilanes and tetraacyloxysilanes derived from o- and p-toluic, o- and p-chlorobenzoic, o-, m-, and p-nitrobenzoic, naphthoic, 2-thiophenecarboxylic, and 2-furoic acids, in the presence of anhydrous aluminum chloride; the results obtained in this series of experiments are given in Table 1.



From Table 1 it is evident that much higher yields of ketones are obtained in the acylation of benzene by acyloxytrichlorosilanes than in acylation by tetraacyloxysilanes; the yields of substituted benzophenones are at least as great as the yields obtained in the acylation of benzene by the corresponding acid chlorides, and therefore acylation by acyloxytrichlorosilanes is certainly of preparative interest. It is very likely that the low yields of chloro- and nitrobenzophenones obtained in the acylation of benzene by tetraacyloxysilanes derived from the

TABLE 1

Yields of Ketones Obtained in the Acylation of Benzene by Tetraacyloxysilanes and Acyloxytrichlorosilanes

		Meaning of R in C_6H_5COR									
		o-$CH_3C_6H_4$	p-$CH_3C_6H_4$	o-ClC_6H_4	p-ClC_6H_4	o-$NO_2C_6H_4$	m-$NO_2C_6H_4$	p-$NO_2C_6H_4$	C_6H_7	C_4H_3O	C_4H_3S
Yield of ketone (in %) on acylation	by tetra-acyloxy-silanes	70	73	35	30	29	44	40	42	30	42
		76	88	70	77	81	76	82	56	45	50

corresponding acids were due to the low solubility of the latter in benzene.

Thiophene was acylated by the acyloxytrichlorosilanes enumerated above, and also by tetraisovaleroxy-, tetrabenzoxy-, tetra-α-naphthoyloxy-, tetra-2-furoyloxy-, and tetra-2-thenoyloxysilanes; the reactions were carried out in benzene in the presence of anhydrous stannic chloride.

TABLE 2

Yields of Ketones Obtained in the Acylation of Thiophene by Tetraacyloxysilanes and Acyloxytrichlorosilanes

		Meaning of R in —COR											
		CH_3	C_2H_5	n-C_3H_7	iso-C_3H_7	n-C_4H_9	iso-C_4H_9	tert-C_4H_9	C_5H_{11}	C_7H_{15}	C_6H_5	$C_{10}H_7$	C_4H_3O	C_4H_3S
Yield of ketone (in %) on acylation	by tetraacyl-oxysilanes	94*	89*	94*	70*	94*	86	57*	95*	70*	73*	53*	21	51
	by acyloxy-trichloro-silanes	95	92	96	80	95	90	75	95	86	80	69	28	60

From Table 2 it is evident that the yields of ketones of the thiophene series obtained on acylation of thiophene by acyloxytrichlorosilanes also exceeded the yields obtained with tetraacyloxysilanes.

EXPERIMENTAL

I. Acylation of Benzene

a) By acyloxytrichlorosilanes. Seventy-five ml of dry benzene and 0.1 mole of the acyloxytrichlorosilane were put into a 200-ml three-neck flask, provided with a powerful stirrer and a reflux condenser with a drying tube, and 18 g (0.13 mole) of anhydrous aluminum chloride was gradually added, the flask being cooled with ice water. Then the mixture was heated in a water bath for 5 hours at 30–50° and for 0.5 hour to boiling, cooled, and poured

*Yields given in the articles by Yu. K. Yur'ev and G. B. Elyakov and co-workers [5,6].

TABLE 3

Yields of Ketones Obtained in the Acylation of Benzene by Acyloxytrichlorosilanes and Tetraacyloxysilanes

Reaction components			Reaction products				
acylating agent		benzene (in ml)	name	melting point	yield (in %)	analytical data	literature data
name	quantity (in g)						
p-Toluyloxytrichlorosilane	27.0	75	p-Methylbenzophenone	58 — 59°	88	Mixture test	M.p. 59° [11]
Tetra-p-toluyloxysilane *	(13.6)	100	p-Methylbenzophenone	58.5— 59	73	Same	
o-Chlorobenzoxytrichlorosilane	29.0	75	o-Chlorobenzophenone	45 — 45.5	70	Found %: Cl 16.23, 16.40. Calculated %: Cl 16.36	M.p. 45.5 [22]
Tetra-o-chlorobenzoxysilane *	(15.6)	100	o-Chlorobenzophenone	45 — 46.5	35	Mixture test	
			o-Chlorobenzoic acid	140 —141	52	Same	
p-Chlorobenzoxytrichlorosilane	29.0	75	p-Chlorobenzophenone	76 — 77	77	Found %: Cl 16.18, 16.41. Calculated %: Cl 16.36	M.p. 75—77 [13]
Tetra-p-chlorobenzoxysilane [1]	16.3	100	p-Chlorobenzophenone	76.5— 77	30	Mixture test	
			p-Chlorobenzoic acid	240 —241	58	Same	
o-Nitrobenzoxytrichlorosilane	30.0	75	o-Nitrobenzophenone	104 —105	81	Found %: N 6.26, 6.28. Calculated %: N 6.16	M.p. 105 [14, 23]
Tetra-o-nitrobenzoxysilane [1]	17.3	100	o-Nitrobenzophenone	104 —105	29	Mixture test	
			o-Nitrobenzoic acid	145 —146	57	Same	
m-Nitrobenzoxytrichlorosilane	30.0	75	m-Nitrobenzophenone	94 — 94.5	76	Found %: N 6.33, 6.37. Calculated %: N 6.16	M.p. 94—95 [14]
Tetra-m-nitrobenzoxysilane *	(16.7)	100	m-Nitrobenzophenone	94 — 95	44	Mixture test	
			m-Nitrobenzoic acid	139 —140	45	Same	

*On acylation by tetraacyloxysilanes prepared in a benzene medium, the yield of acylation products was reckoned on the total quantity of organic acid taken for the preparation of the tetraacyloxysilane (given in parentheses).

Reaction components			Reaction products				
acylating agent							
name	quantity (in g)	benzene (in ml)	name	melting point	yield (in %)	analytical data	literature data
p-Nitrobenzoxytrichlorosilane	30.0	75	p-Nitrobenzophenone	137 —138°	82	Found %: N 5.94, 5.98. Calculated %: N 6.16.	M.p. 138° [15,22]
Tetra-p-nitrobenzoxysilane [1]	17.3	100	p-Nitrobenzophenone	137 —137.5	40	Mixture test	
			p-Nitrobenzoic acid	237 —238	48	Same	
α-Naphthoyloxytrichlorosilane	30.6	75	Phenyl α-naphthyl ketone	75.5— 76	56	Same	M.p. 75.5 [16]
			α-Naphthoic acid	158 —159	30	Same	
Tetra-α-naphthoyloxysilane •	(17.2)	100	Phenyl α-naphthyl ketone	75 — 75.5	42	Same	
			α-Naphthoic acid	158 —159	45	Same	
2-Thenoyloxytrichlorosilane	26.2	75	Phenyl 2-thienyl ketone	56 — 56.5	50	Same	M.p. 55—56 [5]
Tetra-2-thenoyloxysilane •	(12.8)	100	Phenyl 2-thienyl ketone	55.5— 56.5	42	Same	

on ice. The benzene was removed by steam distillation and the heavy residue filtered thru coarse calico. The filtrate and residue were extracted with ether. The ethereal extracts were washed with alkali solution and dried with anhydrous magnesium sulfate. The ether was driven off and the ketone distilled in vacuo or recrystallized.

The acid formed on hydrolysis of the unreacted acyloxytrichlorosilane was isolated from the alkaline extracts by acidification.

b) By tetraacyloxysilanes. The tetraacyloxysilane was prepared from 0.1 mole of acid and 5.1 g (0.03 mole) of silicon tetrachloride in 100 ml of benzene by the method described earlier [5]. The reaction was carried out in the presence of 0.13 mole of anhydrous aluminum chloride, and the reaction product was isolated as described above.

1. o-Methylbenzophenone. a) A 27.0 g quantity of o-toluyloxytrichlorosilane was brought into the reaction. There was obtained 14.9 g (76%).

B.p. 140—141° (5 mm), n_D^{20} 1.5943, d_4^{20} 1.1098, MR_D 60.01. $C_{14}H_{12}O$ F_6. Calculated 59.66.

Found %: C 85.31, 85.35; H 6.30, 6.34. $C_{14}H_{12}O$. Calculated %: C 85.69; H 6.17.

b) A 13.6 g quantity of o-toluic acid was brought into reaction. There was obtained 13.7 g (70%).

B.p. 144—145° (7 mm), n_D^{20} 1.5937, d_4^{20} 1.113, MR_D 59.88. Value of [21]: b.p. 134-137° (2 mm).

2. Phenyl 2-furyl ketone. A 24.5 g quantity of 2-furoyloxytrichlorosilane was brought into reaction. There was obtained 7.75 g (45%).

B.p. 132—133° (5 mm), n_D^{20} 1.6045, d_4^{20} 1.1811, MR_D 50.17. $C_{11}H_8O_2$ F_5 Calculated: 47.92.

Found %: C 76.51, 76.53; H 4.51, 4.44, $C_{11}H_8O$. Calculated %: C 76.72; H 4.68.

b) An 11.2 g quantity of 2-furoic acid was brought into reaction. There was obtained 5.2 g (30%).

B.p. 134—135° (6 mm), n_D^{20} 1.6041, d_4^{20} 1.1817, MR_D 50.08.

Literature data [17]: b.p. 164° (19 mm), n_D^{20} 1.6055, d_4^{20} 1.1839.

The rest of the ketones which were obtained in this series of experiments which consisted of crystalline substances, are given in Table 3.

II. Acylation of Thiophene.

a) By acyloxytrichlorosilanes. Into a 400-ml three-necked flask provided with a stirrer, dropping funnel, and reflux condenser with a drying tube were put 250 ml of

TABLE 4

Yields of Ketones Obtained in the Acylation of Thiophene by Acyloxytrichlorosilanes and Tetraacyloxysilanes

Reaction components			Reaction products							
acylating agent							MR_D			
name	quantity (in g)	thiophene (in g)	name	boiling point (pressure in mm)	n_D^{20}	d_4^{20}	found	calculated	yield (in %)	literature data
Acetoxytrichlorosilane	19.3	8.4	Methyl 2-thienyl ketone	88— 89° (10)	1.5660	1.1747	35.03	34.76	95	B.p. 89.5° (11 mm), n_D^{20} 1.5675, d_4^{20} 1.1750 [5]
Propionoxytrichlorosilane	20.7	8.4	Ethyl 2-thienyl ketone	82— 83 (5)	1.5545	1.1381	39.49	39.40	92	B.p. 81 ° (11 mm), n_D^{20} 1.5675, d_4^{20} 1.1390 [5]
Butyroxytrichlorosilane	22.2	8.4	Propyl 2-thienyl ketone	96— 97 (5)	1.5444	1.1025	44.17	44.00	96	B.p. 89° (3 mm), n_D^{20} 1.5442, d_4^{20} 1.1030 [5]
Isobutyroxytrichlorosilane	22.2	8.4	Isopropyl 2-thienyl ketone	110—111 (10)	1.5459	1.1070	44.11	44.00	80	B.p. 105—107° (8 mm), n_D^{20} 1.5454, d_4^{20} 1.1076 [5]
Valeroxytrichlorosilane	23.6	8.4	n-Butyl 2-thienyl ketone	106—107 (6)	1.5355	1.0749	48.68	48.87	95	B.p. 97° (3 mm), n_D^{20} 1.5363, d_4^{20} 1.0740 [5]
Isovaleroxytrichlorosilane	23.6	8.4	Isobutyl 2-thienyl ketone	92— 93 (5)	1.5323	1.0659	48.93	48.87	90	B.p. 77—90° (2 mm), n_D^{20} 1.5329 [24]
Tetraisovaleroxysilane •	(10.2)	8.4	Isobutyl 2-thienyl ketone	96— 97 (7)	1.5326	1.0653	48.99	48.87	86	
Tetra(trimethylacetoxy) silane	23.6	8.4	tert-Butyl 2-thienyl ketone	101—102 (5)	1.5359	1.0729	48.88	48.87	75	B.p. 113—114° (14 mm), n_D^{20}

•See Footnote to Table 3.

TABLE 4 (continued)

Reaction components			Reaction products							
acylating agent		thiophene (in g)	name	boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		yield (in %)	literature data
name	quantity (in g)						found	calculated		
Caproyloxytrichlorosilane	25.0	8.4	n-Amyl 2-thienyl ketone	119—120° (6)	1.5291	1.0528	53.47	53.23	95	B.p. 110° (3 mm), n_D^{20} 1.5300, d_4^{20} 1.5020 [5]
Caprylyloxytrichlorosilane	27.8	8.4	n-Heptyl 2-thienyl ketone	147—148 (5)	1.5188	1.0142	62.81	62.46	86	B.p. 152—153° (8 mm), n_D^{20} 1.5182, d_4^{20} 1.0110 [7]
Benzoxytrichlorosilane	25.5	8.4	Phenyl 2-thienyl ketone ••	M. p. 56.5—57	—	—	—	—	80	
α-Naphthoyloxytrichlorosilane	30.6	8.4	α-Naphthyl 2-thienyl ketone ••	M. p. 69.5—70	—	—	—	—	69	M.p. 69-170° [7]
2-Furoyloxytrichlorosilane	24.5	8.4	2-Furyl 2-thienyl ketone •••	140—141 (5)	1.6332	1.3217	48.14	47.12	28	B.p. 134—136° (3 mm), n_D^{24} 1.6694, d_{25}^{25} 1.3004 [19]
Tetra-2-furoyloxysilane•	(11.2)	8.4	2-Furyl 2-thienyl ketone	148—149 (9)	1.6343	1.3225	48.21	47.12	21	
2-Thenoyloxytrichlorosilane	26.2	8.4	Di-2-thienyl ketone••••	M. p. 89.5—90	—	—	—	—	60	M.p. 87—89° [20]
Tetra-2-thenoyloxysilane	(12.8)	8.4	Di-2-thienyl ketone ••	M. p. 89—90	—	—	—	—	51	

•See Footnote to Table 3.

••A mixture test with a known sample gave no depression.

•••Found %: C 60.91, 60.74; H 3.57, 3.54. $C_9H_6O_2S$. Calculated %: C 60.66; H 3.40.

••••Found %: C 55.39, 55.38; H 3.26, 3.18. $C_9H_6OS_2$ Calculated %: C 55.64; H 3.11.

dry benzene, 0.1 mole of the acyloxytrichlorosilane, and 0.1 mole of thiophene, after which 0.05 mole of anhydrous stannic chloride in 30 ml of dry benzene was added dropwise, the flask being cooled. The mixture was heated in a water bath for 4 hours at 40–60° and boiled for 15–20 minutes. On cooling, it was decomposed with 100–150 ml of ice water and distilled with steam superheated to 300°. The benzene layer of the distillate was separated, and the water layer was saturated with potash and extracted with ether. The extract was dried with calcium chloride, the solvent driven off, and the ketones distilled in vacuo or recrystallized from alcohol.

b) By tetraacyloxysilanes. In the acylation of thiophene with tetraacyloxysilanes by the method described earlier [5], the reactions were carried out with 0.1 mole of the acid, 0.03 mole of silicon tetrachloride, and 0.1 mole of thiophene in the presence of 0.05 mole of anhydrous stannic chloride.

The ketones obtained in this series of experiments are listed in Table 4.

SUMMARY

1. In the acylation of benzene and thiophene, acyloxytrichlorosilanes are more active acylating agents than tetraacyloxysilanes formed by the same organic acids.

2. Acylation by acyloxytrichlorosilanes, which are quantitatively formed by treating organic acids with an excess of silicon tetrachloride, is a convenient method for the synthesis of ketones of the benzene and thiophene series.

LITERATURE CITED

[1] Yu. K. Yur'ev, Z. V. Belyakova and V. P. Volkov, Zhur. Obshchei Khim. 29, 1463 (1959). •

[2] Yu. K. Yur'ev, Z. V. Belyakova and V. P. Volkov, Zhur. Obshchei Khim. 29, 3652 (1959). •

[3] Yu. K. Yur'ev and Z. V. Belyakova, Zhur. Obshchei Khim. 28, 1755 (1958). •

[4] Yu. K. Yur'ev, G. B. Elyakov, and Z. V. Belyakova, Zhur. Obshchei Khim. 24, 1568 (1954). •

[5] Yu. K. Yur'ev and G. B. Elyakov, Doklady Akad. Nauk SSSR 86, 337 (1952).

[6] Yu. K. Yur'ev, Z. V. Belyakova, and N. S. Zefirov, Zhur. Obshchei Khim. 27, 3264 (1957). •

[7] Yu. K. Yur'ev, G. B. Elyakov, N. S. Zeifirov and A. N. Vysokosov, Zhur. Obshchei Khim. 26, 3341 (1956). •

[8] Yu. K. Yur'ev and G. B. Elyakov, Doklady Akad. Nauk SSSR 102, 763 (1955).

[9] G. Reddelien, Ber. 48, 1468 (1915).

[10] E. Ador and A. Rilliet, Ber. 12, 2299 (1879).

[11] K. Auwers and P. Strödter, Ber. 59, 530 (1926).

[12] F. Mayer, W. Freund and C. Graebe, Ber. 55, 2051 (1922).

[13] R. Demuth and M. Dittrich, Ber. 23, 3609 (1890).

[14] R. Geigy and W. Koenigs, Ber. 18, 2401 (1885).

[15] G. Schroeter, Ber. 42, 3360 (1909).

[16] G. Reddelien, Ber. 46, 2722 (1913).

[17] R. Marquis, Ann. chim. phys. (8) 4, 276 (1905).

[18] R. Scholl and C. Seer, Lieb. Ann. 394, 174 (1912).

[19] H. Gilman, L. Powe and I. Dickey, Rec. trav. Chim. 52, 395 (1938).

[20] F. Blicke and F. Anderson, J. Am. Chem. Soc. 74, 1733 (1952).

[21] I. I. Lapkin and A. I. Golovkova, Zhur. Obshchei Khim. 19, 701 (1949). •

•Original Russian pagination. See C. B. translation.

[22] P. Montagne and S. Koopal, Rec. trav. Chim. 29, 133 (1910).

[23] R. Goncalves, M. Kegelman and E. Brown, J. Org. Ch. 17, 705 (1952).

[24] H. Pines, B. Kvetinskas, J. Veseley and E. Baclawski, J. Am. Chem. Soc. 73, 5173 (1951).

OXIDATION OF UNSYMMETRICAL TETRA- AND TRISUBSTITUTED FURANIDONES-3 BY SELENIUM DIOXIDE

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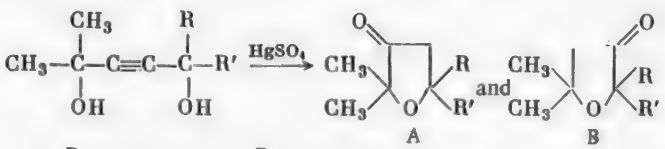
Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp 3880–3884, December, 1959

Original article submitted December 15, 1958

In the preceding articles [1–3] it was shown that the oxidation of 2,2,5,5-tetraalkylfuranidones-3 with identical substituents in positions 2 and 5, by selenium dioxide, is a convenient method of synthesis of the corresponding 2,2,5,5-tetraalkylfuranidinediones-3,4.

In the present work we extended this method to furanidones-3 having different substituents in positions 2 and 5. Since the acetylenic γ-glycols required for their synthesis had an unsymmetrical structure, it was to be expected that the simultaneous hydration and dehydration of the latter under the influence of mercuric sulfate would lead to two isomeric furanidones-3, differing in the position of the carbonyl group relative to one substituent or the other•; 2,2-dimethyl-5,5-tetramethylenefuranidones-3 and -4 (I, structures A and B), which can be formed from 3-methyl-1-(1'-hydroxycyclopentyl)butyn-1-ol-3, and 2,2-dimethyl-5,5-pentamethylenefuranidones-3 and -4 (II, structures A and B), which can be formed from 3-methyl-1-(1'-hydroxycyclohexyl)-butyn-1-ol-3, may serve as examples.

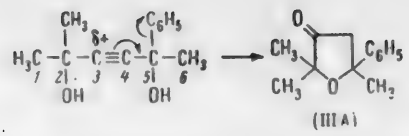


(I) $\overset{R}{R'}\!>\!=\square$; (II) $\overset{R}{R'}\!>\!=\bigcirc$; (III) $R = CH_3$, $R' = C_6H_5$

We found that ketones (I) and (II), which we prepared and which boil within a narrow temperature interval (0.7–1°), form two isomeric 2,4-dinitrophenylhydrazones which may be separated by fractional crystallization. Therefore the formation of unsymmetrically substituted 2,2,5,5-tetraalkylfuranidones-3 from the corresponding acetylenic γ-glycols, actually go in both possible directions and lead to a mixture of two isomers with structures A and B.

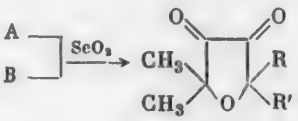
From 2-methyl-5-phenylhexyne-3-diol-2,5 we prepared a ketone forming only one 2,4-dinitrophenylhydrazon Therefore only one of the isomeric ketones is formed in the given case; to it we assign the structure of 2,2,5-trimethyl-5-phenylfuranidone-3 (III, structure A) on the following basis. It is known from work [5] that in the hydration of an unsymmetrical acetylenic γ-glycol, the hydroxyl must add to an electron-deficient carbon atom; in the case of 2-methyl-5-phenylhexyne-3-diol-2,5, owing to the electrophilic character of the benzene nucleus, C^3 is such a carbon atom, and therefore the ketone formed must have structure (IIIA).

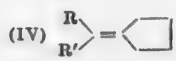
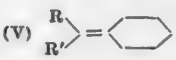
•The indefiniteness of the direction of hydration of the acetylenic bond in unsymmetrical γ-butynediols has already been pointed out in [4].



(IIIA)

The oxidation of a mixture of isomeric furanidones-3 (IA and B; IIA and B) by selenium dioxide led to one 3,4-diketone of the furanidine series.



(IV)  ; (V)  ; (VI) R = CH_3, R′ = C_6H_5

The 2,2-dimethyl-5,5-tetramethylenefuranidinedione-3,4 (IV) and 2,2-dimethyl-5,5-pentamethylenefuranidinedione-3,4 (V) obtained in this way had the form of low-melting bright-crimson hygroscopic crystals which gave white hydrates with water (or on standing in air). 2,2,5-Trimethyl-5-phenylfuranidinedione-3,4 (VI) was a thick, crimson-red liquid; like 2,5-dimethyl-2,5-diphenylfuranidinedione-3,4 [3], it did not form a crystalline dioxime.

In order to establish the limits of applicability of the method, it was necessary to determine the behavior of furanidones-3, having a hydrogen atom in position 2 or 5, in this reaction. From literature data it is known that the oxidation of β-furanidone by selenium dioxide led to opening of the ring at the β,β'-carbon-carbon bond and formation of diglycolic acid [6]; with only one hydrogen atom in position 2, however, as in 2-methyl-5,5-di-p-tolylfuranidone-3, E. D. Venus-Danilova and Z. V. Printseva [7] obtained the normal oxidation product 2-methyl-5,5-di-p-tolylfuranidinedione-3,4, although the yield was low (27%), a certain amount of the correspondingly substituted diglycolic acid also being formed.

In the present work we oxidized 2,2,5-trimethylfuranidone-3 and 2,2-dimethyl-5-phenylfuranidone-3 with selenium dioxide, but they, in contrast to 2-methyl-5,5-di-p-tolylfuranidone-3, did not form furanidinediones-3, 4; in both cases, along with a very small amount of monobasic acids— acetic acid in the first case and benzoic acid in the second— substances were isolated, which were not furanidinediones-3,4 and were not further investigated.

EXPERIMENTAL •

2,2-Dimethyl-5,5-tetramethylenefuranidones-3 and -4 (I, structures A and B). To a boiling mixture of 30 g of 3-methyl-1-(1'-hydroxycyclopentyl)butyn-1-ol-3 (m.p. 53—55°, yield 62%; literature data [8]: m.p. 56—58°) and 200 ml of water in a flask provided with a reflux condenser and a stirrer, a suspension of 15 g of mercuric sulfate in 30 ml of water was added during 10 minutes. After 4.5 hours of boiling, the ketone was removed by steam distillation; the distillate was then saturated with potash and extracted with ether. The ethereal extracts were dried with potash, the ether driven off, and the residue distilled in vacuo. There was obtained 19.7 g (65.5%).

B.p. 64.8—65.8° (3 mm), n_D^{20} 1.4583, d_4^{20} 0.9708, MR_D 45.40; calcd. 45.63.
Found %: C 71.26, 71.04; H 9.63, 9.58; CO 16.71, 16.42, 16.71. $C_{10}H_{16}O_2$. Calculated %: C 71.39; H 9.59; CO 16.65.

A mixture of the 2,4-dinitrophenylhydrazones of ketones (IA and B) was obtained in methanol and resolved by fractional crystallization from methanol and petroleum ether.

a) First isomer— orange-yellow crystals soluble in methanol, petroleum ether, and benzene; m.p. 136—137° (from moist methanol).

Found %: C 54.84, 54.85; H 5.78, 5.94; N 15.76, 15.86. $C_{16}H_{20}O_5N_4$. Calculated %: C 55.16; H 5.79; N 16.08.

•Student L. A. Kuznetsova participated in the experimental part.

b) Second isomer — yellow-orange crystals, slightly soluble in methanol and petroleum ether, very soluble in benzene; m.p. 158.5—159.5° (from a petroleum ether-benzene mixture).

Found %: C 55.63, 55.48; H 6.13, 6.17; N 16.23, 16.06. $C_{16}H_{20}O_5N_4$. Calculated %: C 55.16; H 5.79; N 16.08.

The quantitative ratio of the first isomer to the second was about 10: 1.

2,2-Dimethyl-5,5-pentamethylenefuranidones-3 and -4 (II, structures A and B). Obtained, as described above, by boiling a mixture of 80 g of 3-methyl-1-(1'-hydroxycyclohexyl)butyn-1-ol-3 (m.p. 94.5—95°, yield 83.5%; literature data: m.p. 94—95° [9], 94—95° [10], 98° [11]) and 34 g of mercuric sulfate in 460 ml of water for 8 hours. Yield 64.5 g (80.5%).

B.p. 71.5—72.2° (3 mm), n_D^{20} 1.4632, d_4^{20} 0.9940, MR_D 50.52; calcd. 50.25.
Found %: C 72.82, 72.86; H 10.10, 10.18. $C_{11}H_{18}O_2$. Calculated %: C 72.49; H 9.96.

A mixture of the 2,4-dinitrophenylhydrazones of ketones (IIA and B) was obtained in methanol and resolved by fractional crystallization from the latter.

a) First isomer— yellow needles soluble in boiling methanol, benzine, and benzene; m.p. 159.2—159.3° (from methanol).

Found %: C 56.55, 56.66; H 6.43, 6.39; N 15.16, 15.21. $C_{17}H_{22}O_5N_4$. Calculated %: C 56.35; H 6.12; N 15.46.

b) Second isomer— orange needles, slightly soluble in methanol and benzine and very soluble in benzene; m.p. 228.5—229.5° (from a benzine-benzene mixture).

Found %: C 56.52, 56.56; H 6.25, 6.42; N 15.04, 14.84. $C_{17}H_{22}O_5N_4$. Calculated %: C 56.35; H 6.12; N 15.46.

The quantitative ratio of the first isomer to the second was about 4: 1.

2,2,5-Trimethyl-5-phenylfuranidone-3 (IIIA). This was obtained, as described above, by boiling a mixture of 42 g of 2-methyl-5-phenylhexyne-3-diol-2,5 (m.p. 81.5—82.5°, yield 47%; literature data [12]: m.p. 81.5—82°) and 20 g of mercuric sulfate in 200 ml of water for 15 hours. On cooling, the mixture was saturated with potash, the mercury filtered out, and the filtrate extracted with ether. The ethereal extracts were saturated with hydrogen sulfide, the mercuric sulfide filtered out, and the filtrate washed with 2 N soda solution and water, and dried with magnesium sulfate. After removal of the ether and distillation in vacuo, 23.3 g (55.5%) was obtained.

B.p. 119.5—120° (7 mm), n_D^{20} 1.5083, d_4^{20} 1.0406, MR_D 58.54. $C_{13}H_{16}O_2F_3$ Calculated 58.09.
Found %: C 76.06, 75.86; H 8.04, 8.12. $C_{13}H_{16}O_2$. Calculated %: C 76.44; H 7.90.

2,4-Dinitrophenylhydrazone— orange-yellow needles; obtained in ethanol; m.p. 160—160.5° (from a petroleum ether-benzene mixture).

Found %: C 59.35, 59.32; H 5.33, 5.48; N 14.82, 14.76. $C_{19}H_{20}O_5N_4$. Calculated %: C 59.37; H 5.24; N 14.58.

On fractional crystallization from alcohol the second isomer was not found.

2,2-Dimethyl-5,5-tetramethylenefuranidinedione-3,4 (IV). To a boiling solution of 14 g (0.126 mole) of selenium dioxide in 10 ml of water and 200 ml of dioxane, in a flask provided with reflux condenser, dropping funnel, and stirrer, 16.8 g (0.1 mole) of (I) (mixture of A and B) was added dropwise during 0.5 hour, after which boiling was continued for 12 hours. The selenium was filtered off and washed with dioxane. The dioxane was distilled from the combined filtrates, the residue dissolved in ether and dried with calcium chloride, the ether driven off, and the residue distilled in vacuo. There was obtained 15 g (82.5%) of a hygroscopic, bright-crimson liquid which crystallized on standing; b.p. 86—87° (3 mm), m.p. 29.5—30°.

Found %: C 65.83, 65.50; H 7.92, 7.94. $C_{10}H_{14}O_3$. Calculated %: C 65.91; H 7.74.

On standing briefly in air it was converted to a white hydrate.

Dioxime of compound (IV). A mixture of 2.7 g (0.015 mole) of (IV), 2.1 g (0.03 mole) of hydroxylamine hydrochloride, and 15 ml of anhydrous ethanol was boiled for 5 hours, cooled, and poured into 50 ml of water. There was obtained 3.1 g (about 100%); m.p. 206–206.5° (dec.; from dilute ethanol).

Found %: N13.24, 13.08 $C_{10}H_{16}O_3N_2$. Calculated % N 13.20

2-2-Dimethyl-4,4-tetramethylenefuranidino-(3,4)-quinoxaline. On fusion of 1.8 g (0.01 mole) of (IV) with 1.05 g (0.0097 mole) of o-phenylenediamine there was obtained 2.45 g (about 100%); m.p. 106° (from dilute methanol).

Found %: C 75.60, 75.59; H 7.20, 7.20; N 11.16, 11.19. $C_{16}H_{18}ON_2$. Calculated %: C 75.56; H 7.13; N 11.02.

2,2-Dimethyl-5,5-pentamethylenefuranidinedione-3,4 (V). Obtained, as described above, when a mixture of 12.75 g (0.07 mole) of (II) (mixture of A and B) and 7.8 g (0.07 mole) of selenium dioxide in 2.5 ml of water and 100 ml of dioxane was boiled for 6.5 hours. The diketone distilled at 98–100° (4 mm) and crystallized in the receiver; m.p. 68.5–70° (from petroleum ether and after sublimation in vacuo); hygroscopic, crimson crystals. Yield 12.0 g (87.5%).

Found %: C 67.58, 67.67; H 8.03, 8.03. $C_{11}H_{16}O_3$. Calculated %: C 67.32; H 8.22.

Dioxime of compound (V). From 0.98 g (0.005 mole) of (V), 2.1 g (0.03 mole) of hydroxylamine hydrochloride, 15 ml of pyridine, and 5 ml of anhydrous alcohol there was obtained, as described above, 1.08 g (95.5%); in an evacuated capillary, m.p. 198° (dec.; from dilute ethanol and after sublimation in vacuo); in a nonevacuated capillary, m.p. 187–188° (dec.).

Found %: C 58.72, 58.57; H 8.38, 8.40; N 12.08, 12.29. $C_{11}H_{18}O_3N_2$. Calculated %: C 58.39; H 8.02; N 12.38.

2,2-Dimethyl-4,4-pentamethylenefuranidino-(3,4)-quinoxaline. On fusion of 1.05 g (0.0053 mole) of (V) with 0.55 g (0.005 mole) of o-phenylenediamine there was obtained 1.25 g (93%); m.p. 127° (from methanol).

Found %: C 76.18, 76.23; H 7.72, 7.73; N 10.89, 10.78. $C_{17}H_{20}ON_2$. Calculated %: C 76.08; H 7.51; N 10.44.

2,2,5-Trimethyl-5-phenylfuranidinedione-3,4 (VI). When 10.2 g (0.05 mole) of (IIIA) and 7.8 g (0.07 mole) of selenium dioxide in 4 ml of water and 150 ml of dioxane were boiled for 14 hours, 9.22 g (84.5%) of a viscous, crimson-red liquid was obtained.

B.p. 110° (2 mm), n_D^{20} 1.5140, d_4^{20} 1.1066.

In view of the impossibility of isolating it in an analytically pure state, it was characterized through the quinoxaline derivative.

2,2,4-Trimethyl-4-phenylfuranidino-(3,4)-quinoxaline. A 4.6 g quantity (0.0211 mole) of (VI) and 2.26 g (0.0209 mole) of o-phenylenediamine in 25 ml of alcohol were boiled for 30 minutes and poured into 50 ml of water. The yellow oil was extracted with ether and the extract dried with potash. The ether was driven off and the residue distilled in vacuo; the 170–180° (0.5 mm) fraction crystallized on trituration with petroleum ether. Yield 4.15 g (68.5%). The substance was dissolved in a large volume of petroleum ether and filtered, the filtrate evaporated to dryness, and the residue dissolved in anhydrous benzene and twice chromatographed on aluminum oxide. It was eluted with anhydrous benzene. From the eluate a white substance, readily soluble in the usual organic solvents, was isolated; m.p. 73.1–74.6°.

Found %: C 78.55, 78.64; H 6.59, 6.54; N 9.84, 9.66. $C_{19}H_{18}ON_2$. Calculated %: C 78.59; H 6.25; N 9.65.

SUMMARY

1. The isomerization of unsymmetrical ditertiary acetylenic γ-glycols under the influence of mercuric sulfate leads to the formation of a mixture of isomeric furanidones, provided the substitutents in the acetylenic γ-glycols have identical electrodotic properties.

2. The oxidation of furanidones-3 to furanidinediones-3,4 by selenium dioxide goes smoothly if the carbon atoms in positions 2 and 5 of the ring are tertiary. In the presence of a secondary carbon atom in position 2 or 5 of the ring, oxidation with selenium dioxide does not always lead to the corresponding 3,4-diketones of the furanidine series.

LITERATURE CITED

[1] I. K. Korobitsyna, Yu. K. Yur'ev and O. L. Nefedova, Zhur. Obshchei Khim. 24, 188 (1954). •

[2] I. K. Korobitsyna, Yu. K. Yur'ev, Yu. A. Cheburkov, and E. M. Lukina, Zhur. Obshchei Khim. 25, 734 (1955). •

[3] I. K. Korobitsyna, Yu. K. Yur'ev, and K. V. Kuznetsova, Zhur. Obshchei Khim. 27, 1792 (1957). •

[4] H. Henecka, Med. u. Chem. Abhandl. med. Chem. Forschungsstätten, J. G. Farbenind. 3, 403 (1936); C. A, 31, 5792 (1937).

[5] I. N. Nazarov and I. V. Torgov, Zhur. Obshchei Khim. 18, 1322 (1948).

[6] I. K. Korobitsyna, Yu. K. Yur'ev, and E. M. Lukina, Zhur. Obshchei Khim. 25, 563 (1955). •

[7] E. D. Venus-Danilova and Z. V. Printseva, Zhur. Obshchei Khim. 26, 2170 (1956). •

[8] Yu. S. Zal'kind and I. M. Gverdtsiteli, Zhur. Obshchei Khim 9, 855 (1939).

[9] A. T. Babayan, Zhur. Obshchei Khim. 10, 1177 (1940).

[10] A. T. Babayan, Zhur. Obshchei Khim. 10, 480 (1940).

[11] A. T. Babayan, Izvest. Akad. Nauk Armyan. SSR 1941, 121; C. A. 40, 3394 (1946).

[12] Yu. S. Zal'kind and A. P. Ivanov, Zhur. Obshchei Khim. 11, 803 (1941).

•Original Russian pagination. See C. B. translation.

ETHYLENE SULFIDE IN THE SYNTHESIS OF HETEROCYCLIC COMPOUNDS WITH TWO HETEROATOMS

X. CONDENSATION OF β-MERCAPTOETHYLAMINE WITH HETEROCYCLIC ALDEHYDES, ISONITROSOACETONE, AND PYRUVIC ACID

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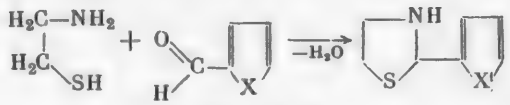
Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp 3885-3888, December 25, 1959

Original article submitted December 25, 1958

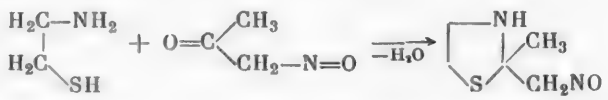
In one of our papers [1] it was shown that β-mercaptoethylamine with an aryl group on the nitrogen atom condenses with heterocyclic aldehydes—furfural, thiophene-2-aldehyde, and selenophene-2-aldehyde— forming the corresponding 3-arylthiazolidines with the furyl, thienyl, or selenienyl substituents in position [2]. In 1953, Tsukerman ∂ tried to carry out the condensation of β-mercaptoethylamine hydrochloride with furfural and thus obtain 2-(furyl)thiazolidine, but this did not occur. We have suggested in this connection [1] that the actual reason for this failure is the instability in an acid medium of the reaction product, a thiazolidine with the furyl radical in position 2. Therefore, in the present work, in the condensation with furfural, and also with thiophene-2-aldehyde and selenophene-2-aldehyde, we added free β-mercaptoethylamine (cysteamine) and, as expected, obtained the corresponding thiazolidine with a yield of 40—80%.



X = O, S, Se

The thiazolidines obtained in this way with heterocyclic radicals in position 2 are unstable compounds which are very easily decomposed even in the cold and in the dark, so that we were unable to carry out the elementary analysis of 2-(2'-selenienyl)thiazolidine, which was the least stable compound.

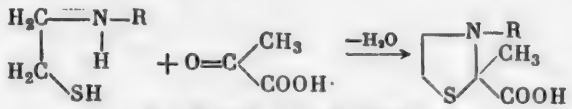
The synthesis which we previously described of 2-acyl-3-arylthiazolidines by condensation of N-(β-mercaptoethyl)arylamines with α-ketoaldehydes [3] under mild conditions was based on the fact that ketones undergo an analogous reaction with β-mercaptoethylamines [4] under much more severe conditions than do aldehydes. However, in the present work we have shown that some compounds which contain the ketone group react with β-mercaptoethylamine as easily as aldehydes. Thus, when β-mercaptoethylamine condenses with methyl glyoxal monooxime, isonitrosoacetone, we obtain 2-methylthiazolidine-2- aldehydeoxime:



Evidently, in this concentration the isonitrosoacetone reacts in its nitroso form, that is, the same as with ethyl mercaptan [5] or aniline [6].

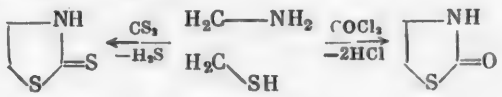
Attempts to convert our oxime into the nitrile of 2-methylthiazolidine-2-carboxylic acid did not give positive results: the action of acetic anhydride gave only tarry products.

It is very easy to bring about the condensation of the α-ketoacid pyruvic acid. In the reaction of pyruvic acid with β-mercaptoethylamine or N-(β-mercaptoethyl)arylamines we obtained the corresponding 2-methylthiazolidine-2-carboxylic acids with a yield of 70-93%.



R = H, C_6H_5, o- and p-$CH_3C_6H_4$

The condensations which we studied previously of N-(β-mercaptoethyl)arylamines with carbon disulfide [7] and with phosgene [8] proceeded smoothly and gave good yields of the corresponding 3-arylated 2-thiazolidinethiones and 2-thiazolidones. In the present work, which describes the analogous reaction with β-mercaptoethylamine, we have shown that condensation with carbon disulfide goes smoothly and gives 65% yields of the 2-thiazolidinethione, while in the condensation with phosgene the 2-thiazolidone was obtained only in small yields (22%) and the chief reaction product was a highly polymerized, viscous substance, which contained halogen and did not give a reaction for the sulfhydryl group. It was not studied further.



EXPERIMENTAL

2-(2'-Furyl)thiazolidine. A mixture of 3.08 g β-mercaptoethylamine in 50 ml of dry benzene and 3.84 g of furfural was boiled in a Dean-Stark apparatus until evolution of water stopped. After the benzene had been distilled off, the oily residue was extracted for 15 hours with ligroin (b.p. 30–50°) in an extractor. After distillation of the ligroin, we obtained 5 g (80%) of 2-(2'-furyl)thiazolidine, m.p. 54–55° (fom ligroin); colorless crystals which sublimed at 30–34° (9 mm), easily soluble in alcohol, ether, acetone, benzene, dichloroethane, poorly soluble in water; decomposed rapidly on standing.

Found %: C 54.20, 54.25; H 5.96, 5.91; N 8.85, 9.04. C_7H_9ONS. Calculated %: C 54.16; H 5.84; N 9.02.

2-(2'-Thienyl)thiazolidine. To 0.77 g β-mercaptoethylamine in 10 ml of anhydrous alcohol we added 1.12 g of thiophene-2-aldehyde and allowed the mixture to stand 72 hours at room temperature. After distilling off the alcohol in a vacuum, we obtained a residue which crystallized in colorless needles which were then sublimed in a vacuum and recrystallized from ligroin; m.p. 41.5–42.5°. Yield 0.74 g (43%). Solubility similar to that of the previous compound. Very quickly decomposed on standing.

Found %: C 49.61; H 5.33; N 7.76. $C_7H_9NS_2$. Calculated %: C 49.08; H 5.30; N 8.18.

2-(2'-Selenienyl)thiazolidine. To 0.77 g of β-mercaptoethylamine in 10 ml of anhydrous alcohol we added 1.59 g of selenophene-2-aldehyde. After 48 hours (from the disappearance of the reaction for sulfhydryl groups) the alcohol was removed in a vacuum and the residue which crystallized was sublimed in a vacuum and recrystallized from ligroin; m.p. 42–43°. Yield 0.83 g (40%). Solubility was like that of the previous substances. Decomposed especially quickly on standing, and particularly on heating, so that we could obtain only approximate data for the elementary analysis.

Thiazolidine-2-aldehyde oxime. To 1.93 g of β-mercaptoethylamine in 10 ml of anhydrous alcohol we added a solution of 2.18 g of isonitrosoacetone in 3 ml of anhydrous alcohol and heated the mixture to boiling. When the alcohol had cooled, the solvent was distilled off in a vacuum. We obtained 0.85 g (23%); m.p. 115.5–116° (from alcohol).

Found %: C 41.44, 41.34; H 6.96, 7.11; N 19.32, 19.46. $C_5H_{10}ON_2S$. Calculated %: C 41.07; H 6.89; N 19.16.

2-Methylthiazolidine-2-carboxylic acid. To 0.77 g of β-mercaptoethylamine we added 0.88 g of pyruvic acid. The reaction occurred with strong spontaneous heating. Colorless crystals precipitated when the solution was cooled. We obtained 1.37 g (93%) with m.p. 176-177° (decomposition; from 75% alcohol).

Found %: C 41.00, 41.04; H 6.21, 6.27; N 9.28, 9.46. M 146.1, 150.7. $C_5H_9O_2NS$. Calculated %: C 40.79; H 6.16; N 9.51. M 147.2.

The acid was easily soluble in water and dioxane, poorly soluble in alcohol, insoluble in ether, acetone, benzene, dichloroethane, and ligroin.

2-Methyl-3-phenylthiazolidine-2-carboxylic acid. From 0.77 g of N-(β-mercaptoethyl)aniline and 0.44 g of pyruvic acid we obtained as described above 0.83 g (74.5%), m.p. 155.5—156.5° (from benzene). Easily soluble in ether, acetone, dioxane, dichloroethane, poorly soluble in alcohol, insoluble in water.

Found %: C 59.34; H 6.09; N 6.33, 6.29. $C_{11}H_{13}O_2NS$. Calculated %: C 59.16; H 5.87; N 6.27.

2-Methyl-3-p-tolylthiazolidine-2-carboxylic acid. From 0.84 g of N-(β-mercaptoethyl)-p-toluidine and 0.44 g of pyruvic acid we obtained as described above 0.84 g (70.5%) with a m.p. 155—156°. Easily soluble in ether, acetone, dioxane, dichloroethane, poorly soluble in alcohol, insoluble in water.

Found %: C 60.93, 61.00; H 6.57, 6.58; N 5.98, 6.00. $C_{12}H_{15}O_2NS$. Calculated %: C 60.73; H 6.37; N 5.90.

2-Methyl-3-o-tolylthiazolidine-2-carboxylic acid. From 0.84 g of N-(β-mercaptoethyl)-o-toluidine and 0.44 g of pyruvic acid we obtained as described above 0.93 g (78%) with m.p. 121—122° (decomposition; from ligroin). Easily soluble in ether, acetone, dichloroethane, poorly soluble in alcohol, insoluble in water.

Found %: C 60.88; H 6.56; N 6.07, 6.17. $C_{12}H_{15}O_2NS$. Calculated %: C 60.73; H 6.37; N 5.90.

2-Thiazolidinethione. The mixture of 1.93 g (0.025 g-mole) of β-mercaptoethylamine in 10 ml of anhydrous alcohol, 1.4 g (0.025 g-mole) potassium hydroxide, and 3.8 g (0.05 g-mole) carbon disulfide was boiled 4 hours. After distilling off the excess carbon disulfide and alcohol we washed the crystals of orange residue on the filter with cold water until they were colorless (the filtrate was evaporated to a volume of 2—3 ml and the crystals which again precipitated were added to the main mass). We obtained 1.95 g (65.5%) m.p. 105—105.5° (from methyl alcohol). A sample mixed with known 2-thiazolidinethione showed no depression of melting point.

The literature gives m.p. 105—106° [9].

2-Thiazolidone. To a solution of 1.93 g (0.025 g-mole) of β-mercaptoethylamine in 60 ml of toluene we added with stirring 18.5 ml of 20% solution of phosgene in toluene and the mixture was heated for 15 minutes. Then the toluene solution was separated from the layer of viscous oil, and after distillation of the toluene we obtained 0.57 g (22%) with m.p. 52.5—53° (from ether).

Found %: C 35.05, 35.23; H 4.92, 4.90; N 13.18, 13.23. C_3H_5ONS. Calculated %: C 34.93; H4.89; N13.58.

The literature gives m.p. 54° [10]; 50—52° [11].

SUMMARY

1. Condensation of β-mercaptoethylamine with furfural, thiophene-2-aldehyde, and selenophene-2-aldehyde gives the corresponding 2-(2'-furyl)-, 2-(2'-thienyl)-, and 2-(2'-selenienyl)thiazolidine, which are unstable compounds.

2. Reaction of β-mercaptoethylamine with isonitrosoacetone gives 2-methylthiazolidine-2-aldehyde oxime.

3. Condensation of β-mercaptoethylamine and its N-aryl derivatives with pyruvic acid gives 2-methylthiazolidine-2-carboxylic acids with yields of 70—93%.

4. When β-mercaptoethylamine is condensed with carbon disulfide or phosgene it forms 2-thiazolidinethione (65%) and 2-thiazolidone (22%), respectively.

LITERATURE CITED

[1] Yu. K. Yur'ev and S. V. Dyatlovitskaya, Zhur. Obshchei Khim. 28, 2377 (1958). •

[2] S. V. Tsukerman, Ukrain. Khim. Zhur. 19, 169 (1953).

[3] Yu. K. Yur'ev and S. V. Dyatlovitskaya, Khim. Nauka i Prom. 2, 806 (1957); Zhur. Obshchei Khim. 29, 1083 (1959). •

•Original Russian pagination. See C. B. translation.

[4] S. V. Tsukerman, Ukrain. Khim. Zhur. 19, 523 (1953).

[5] T. Posner, Ber. 32, 1241 (1899).

[6] R. Holleman, Rec. trav. chim. 10, 223 (1891).

[7] Yu. K. Yur'ev and S. V. Dyatlovitskaya, Zhur. Obshchei Khim. 27, 3152 (1957). •

[8] Yu. K. Yur'ev and S. V. Dyatlovitskaya, Zhur. Obshchei Khim. 27, 2644 (1957). •

[9] L. Knorr and P. Rössler, Ber. 36, 1281 (1903).

[10] J. Crawhall and D. Elliot, J. Chem. Soc. 1952, 3094.

[11] J. Michels and G. Gwen, J. Am. Chem. Soc. 78, 5349 (1956).

•Original Russian pagination. See C. B. translation.

DOUBLE DIAZONIUM SALTS OF THE TYPE $Ar_2SbCl \cdot ArN_2Cl$

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3857-3866, December, 1959

Original article submitted October 27, 1958

One of us [1] previously obtained double diazonium salts of antimony pentachloride and metalloorganic compounds of pentavalent antimony. The preparation of these salts offered new possibilities for the synthesis of antimony-organic compounds of the aromatic series [2–5].

We decided to use also double diazonium salts of diarylchlorostibines, $Ar_2SbCl \cdot ArN_2Cl$, for the synthesis of antimony-organic compounds. The sole example of this type of salt is the double salt of diphenylchlorostibine and phenyldiazonium chloride described by Bruker and Nikiforova [6].

This double salt, according to the data of these authors, was obtained by pouring together an acetic acid solution of diphenylchlorostibine and phenyldiazonium chloride; it was obtained as a grayish powder, which dissolved in acetone with decomposition and gave diphenylantimony trichloride when it was decomposed in chloroform and dilute hydrochloric acid.

Frequent repetition of this work showed us that under the conditions described in [6] the double salt of diphenylchlorostibine and phenyldiazonium chloride $(C_6H_5)_2SbCl \cdot C_6H_5N_2Cl$ was not formed. Under these conditions there was formed only the double salt of phenyldiazonium chloride and diphenyl antimony trichloride, $(C_6H_5)_2SbCl_3 \cdot C_6H_5N_2Cl$; evidently the authors had this salt in impure form and erroneously took it for the double diazonium salt of diphenylchlorostibine.

An entirely analogous result was obtained in the reaction of o-tolyldiazoniumchloride with diphenylchlorostibine: in this case also we found oxidation of the diphenylchlorostibine and formation of $(C_6H_5)_2SbCl_3 \cdot o\text{-}CH_3C_6H_4N_2Cl$.

Decomposition of $(C_6H_5)_2SbCl_3 \cdot C_6H_5N_2Cl$ and $(C_6H_5)_2SbCl_3 \cdot o\text{-}CH_3C_6H_4N_2Cl$ in chloroform and in dilute hydrochloric acid gives, as Bruker describes, diphenyl antimony trichloride. Both double salts are colorless in the pure form.

All our following attempts to obtain double diazonium salts of diphenylchlorostibine (by exchange reactions of diphenylchlorostibine with the double diazonium salts of ferric chloride, zinc chloride, antimony chloride, and also reaction with solid aryldiazonium chlorides) always produced only the double diazonium salt of diphenyl antimony trichloride. Thus, we studied in detail the reaction of diphenylchlorostibine with the double diazonium salts of ferric chloride, which in the case of $ArSbCl_4$ [7], $ArSbCl_3$ [8], and $ArSbCl_2$ [9] smoothly produced the corresponding double diazonium salts of the aryl antimony chloride. As a result of this reaction the double diazonium salt of diphenyl antimony trichloride was formed.

The yield, (calculated on the diphenylchlorostibine taken) and some properties of the salts obtained in this way are given in Table 1.

When we used the double diazonium salts of zinc chloride instead of those of ferric chloride, we also obtained the double diazonium salts of diphenyl antimony trichloride. The yields (calculated on the diphenylchlorostibine taken) and some of the properties of the salts obtained in this way are given in Table 2.

The reason that the results of all the reactions which we studied gave only salts of the type $Ar_2SbCl_3 \cdot ArN_2Cl$ (and not $Ar_2SbCl \cdot ArN_2Cl$) is probably the especially easy oxidation of diphenylchlorostibine into compounds of

TABLE 1.

Double diazonium salt	Melting Point (decomp)	Color	Yield %
$(C_6H_5)_2SbCl_3 \cdot C_6H_5N_2Cl$	148—162°	Colorless	71
$(C_6H_5)_2SbCl_3 \cdot o\text{-}ClC_6H_4N_2Cl$	146—148	Colorless	67
$(C_6H_5)_2SbCl_3 \cdot p\text{-}ClC_6H_4N_2Cl$	146—147	Colorless	72
$(C_6H_5)_2SbCl_3 \cdot o\text{-}CH_3C_6H_4N_2Cl$	165—167	Colorless	75
$(C_6H_5)_2SbCl_3 \cdot p\text{-}CH_3C_6H_4N_2Cl$	128—130	Colorless	89
$(C_6H_5)_2SbCl_3 \cdot o\text{-}CH_3OC_6H_4N_2Cl$	171—174	Rose	97
$(C_6H_5)_2SbCl_3 \cdot p\text{-}CH_3OC_6H_4N_2Cl$	153	Colorless	85
$(C_6H_5)_2SbCl_3 \cdot o\text{-}C_2H_5OC_6H_4N_2Cl$	163	Light yellow	55

pentavalent antimony under the action of different oxidizing agents present in the reaction mixture (oxides of nitrogen, ferric chlorate, oxygen of the air) • Moreover, phenyldiazonium chloride itself apparently acts on diphenylchlorostibine as an oxidant, as is indicated by the following facts: a) violent evolution of nitrogen in all cases; b) increased yield of double salt when there is an excess of the double diazonium salt of zinc chloride; c) obtaining the double diazonium salt of diphenyl antimony trichloride in the reaction of diphenylchlorostibine with the double diazonium salt of zinc chloride in a stream of carbon dioxide, which excludes the catalytic oxidation by oxygen of the air in the presence of zinc chloride; d) obtaining the double diazonium salt of diphenyl antimony trichloride in the reaction of diphenylchlorostibine with solid phenyldiazonium chlorides. The latter reaction proceeds with strong evolution of nitrogen according to the scheme:

$$(C_6H_5)_2SbCl + 3C_6H_5N_2Cl \xrightarrow{\text{alcohol}} (C_6H_5)_2SbCl_3 \cdot C_6H_5N_2Cl + 2N_2 + [2C_6H_5]^{**}\cdot$$

TABLE 2.

Double diazonium salt	Melting Point (decomp)	Color	Yield %
$(C_6H_5)_2SbCl_3 \cdot C_6H_5N_2Cl$	144 —167°	Colorless	73
$(C_6H_5)_2SbCl_3 \cdot p\text{-}CH_3OC_6H_4N_2Cl$	152 —153	Colorless	80
$(C_6H_5)_2SbCl_3 \cdot p\text{-}(CH_3)_2NC_6H_4N_2Cl$	145.5—146.5	Clear yellow	88

The yield of double salt (71%) was calculated on the phenyl diazonium chloride taken in the reaction.

As to the mechanism of the reaction, there is probably first an oxidation of the diphenylchlorostibine to diphenyl antimony trichloride, and then the formation of the double salt ***.

•This idea was confirmed by special experiments.

•• We did not make a special study of the fate of the phenyl radicals. Apparently, as usual, they react with the solvent, giving benzene.

•••We should mention that the compound $(o\text{-}ClC_6H_4)_2SbCl$ in reaction with the phenyldiazonium chloride and with the double diazonium salt of ferric chloride is not oxidized and does not give a double salt. In both cases we recover the starting di-o-chlorophenylstibine.

Since phenyldiazonium chloride can easily oxidize diphenylchlorostibine, we can also consider it probable that the double salt $(C_6H_5)_2SbCl \cdot C_6H_5N_2Cl$ in general cannot exist under ordinary conditions.

EXPERIMENTAL

1. Reaction of diphenylchlorostibine with phenyldiazonium chloride and with o-tolyldiazonium chloride and decomposition of the resulting salts in dilute hydrochloric acid and in chloroform. a) We treated 0.55 g (0.0059 g-mole) of aniline with 2 ml of concentrated hydrochloric acid, added 1.5 g of ice, and diazotized with a solution of 0.7 g (0.101 g-mole) of sodium nitrite in 2 ml of water. At the end of the diazotization we added 10 ml of glacial acetic acid and with cooling to minus 2–3° we added gradually, with stirring, a solution of 1.75 g (0.0056 g-mole) of diphenylchlorostibine in 15 ml of glacial acetic acid; this produced evolution of gas and precipitation of a white precipitate which was the double salt of phenyldiazonium chloride and diphenyl antimony trichloride. The precipitate was filtered, washed with glacial acetic acid, alcohol, and ether. Yield 2.2 g (75%). After reprecipitation from acetone by ether: m.p. 148–162° (with decomposition).

Found %: C 40.81, 41.02; H 3.10, 3.10; Sb 23.57, 23.51. $C_{18}H_{15}N_2Cl_4Sb$. Calculated %: C 41.34; H 2.89; Sb 23.29.

b) The same experiment, but sodium nitrite was halved, and before adding the diphenylchlorostibine the solution was cooled to minus 3–5°. Yield 1.3 g (44%). M.p. 148–164° (with decomposition).

Found %: Sb 23.37, 23.45. $C_{18}H_{15}N_2Cl_4Sb$. Calculated %: Sb 23.29.

The double salt of phenyldiazonium chloride and diphenyl antimony trichloride (0.25 g) was boiled with 4 ml of 5 N hydrochloric acid. Evolution of nitrogen occurred and a small amount of oil formed, which was filtered and not identified. When the filtrate was cooled, crystals of diphenyl antimony trichloride precipitated. Yield 0.13 g (71%). M.p. 172–173°; literature data [6]: m.p. 172–173°.

The double salt of phenyldiazonium chloride and diphenyl antimony trichloride (0.7 g) was boiled in 30 ml of dry chloroform for 6 hours; the solution then became clear. The chloroform was evaporated, the residue was dissolved in alcohol and hydrolyzed with 5% ammonia with ice cooling. The precipitate was filtered off and washed with alcohol and ether. The weight of diphenylstibinic acid was 0.3 g (73%). Recrystallization from 5 N hydrochloric acid gave diphenyl antimony trichloride with m.p. 172–175°; literature data [10]: m.p. 175°.

c) From 1.19 g (0.0111 g-mole of o-toluidine and 3.5 g (0.0112 g-mole) diphenylchlorostibine under the conditions of experiment (a) we obtained 4.2 g of double salt of o-tolyldiazonium chloride and diphenyl antimony trichloride. Yield 70%, m.p. 138–158° (with decomposition).

Found %: C 42.74, 42.89; H 3.18, 3.27; Sb 22.31, 22.42. $C_{19}H_{17}N_2Cl_4Sb$. Calculated %: C 42.50; H 3.19; Sb 22.69.

The double salt of o-tolyldiazonium chloride and diphenyl antimony trichloride (2.5 g) was boiled for 8 hours in chloroform, but the solution did not become clear. The chloroform was evaporated, the residue was dissolved in alcohol, and hydrolyzed with 5% ammonia solution cooled with ice. The precipitate was filtered off, washed with water, pressed out well and washed with alcohol and ether. The precipitate which did not dissolve in ether was diphenyl stibinic acid and was boiled with 5 N hydrochloric acid. The solution was filtered hot. When the filtrate cooled, crystals of diphenyl antimony trichloride separated. Weight 0.45 g (25%). M.p. 169–174°; literature data [6]: m.p. 172–173°. Mixed melting point with the known diphenyl antimony trichloride gave no depression.

2. Reaction of diphenylchlorostibine with the double diazonium salt of ferric chloride. a) One g (0.0032 g-mole) of diphenylchlorostibine was dissolved in 2–3 ml of alcohol saturated with hydrogen chloride, and with ice cooling a saturated solution of 1.07 g (0.0035 g-mole) of the double salt of phenyldiazonium chloride and ferric chloride in 2 ml of anhydrous acetone was added. Evolution of gas occurred. The double salt of phenyldiazonium chloride and diphenyl antimony trichloride which precipitated was filtered off, washed with alcohol and ether. Yield 1 g (59%). After reprecipitation by ether from acetone, m.p. 148–158° (with decomposition).

Found %: C 41.33, 41.12; H 2.92, 2.84; Sb 23.51, 23.32. $C_{18}H_{15}N_2Cl_4Sb$. Calculated %: C 41.34; H 2.89; Sb 23.29.

b) From 1 g (0.0032 g-mole) of diphenyldichlorostibine and 1.5 g (0.0047 g-mole) of the double salt of o-tolyldiazonium chloride and ferric chloride, under the conditions of the previous experiment, we obtained 1.2 g

of the double salt of o-tolyldiazonium chloride and diphenyl antimony trichloride. Yield 70%. After reprecipitation from acetone by ether, m.p. 166–167° (with decomposition).

Found %: Sb 22.89, 22.93. $C_{19}H_{17}N_2Cl_4Sb$ Calculated %: Sb 22.69.

c) From 1 g (0.0032 g-mole) of diphenylchlorostibine and 1.5 g (0.0047 g-mole) of the double salt of para-tolyldiazonium chloride and ferric chloride under the conditions of experiment (a) we obtained 1.5 g of the double salt of p-tolyldiazonium chloride and diphenyl antimony trichloride. Yield 87%. After reprecipitation by ether from acetone, m.p. 128–130° (with decomposition).

Found %: Sb 22.76, 22.63. $C_{19}H_{17}N_2Cl_4Sb$. Calculated %: Sb 22.69

d) From 1 g (0.0032 g-mole) of diphenylchlorostibine and 1.88 g (0.0056 g-mole) of the double salt of o-anisyldiazonium chloride and ferric chloride, under the conditions of experiment (a), we obtained 1.7 g of the double salt of o-anisyldiazonium chloride and diphenyl antimony trichloride. Yield 95%. After reprecipitation by ether from acetone, m.p. 164–167° (with decomposition).

Found %: C 41.03, 41.19; H 3.36, 3.34; Sb 22.26, 22.19. $C_{19}H_{17}ON_2Cl_4Sb$. Calculated %: C 41.28; H 3.10; Sb 22.03.

e) From 1 g (0.0032 g-mole) of diphenylchlorostibine and 1.88 g (0.0056 g-mole) of the double salt of p-anisyldiazonium chloride and ferric chloride under the conditions of experiment (a) we obtained 1.5 g of the double salt of p-anisyldiazonium chloride and diphenyl antimony trichloride. Yield 84%. M.p. 147–148° (with decomposition).

Found %: Sb 22.81, 22.52. $C_{19}H_{17}ON_2Cl_4Sb$. Calculated %: Sb 22.03.

f) From 1 g (0.0032 g-mole) of diphenylchlorostibine and 1.5 g (0.0043 g-mole) of the double salt of o-phenetidyldiazonium chloride and ferric chloride, under the conditions of experiment (a), we obtained 1 g of the double salt of o-phenetidyldiazonium chloride and diphenyl antimony trichloride. Yield 55%. M.p. 163° (with decomposition).

Found %: Sb 21.52, 21.50. $C_{20}H_{19}ON_2Cl_4Sb$. Calculated %: Sb 21.49.

g) From 1 g (0.0032 g-mole) of diphenylchlorostibine and 1.11 g (0.0032 g-mole) of the double salt of o-chlorophenyldiazonium chloride and ferric chloride, under the conditions of experiment (a), we obtained 1.2 g of the double salt of o-chlorophenyldiazonium chloride and diphenyl antimony trichloride. Yield 67%. M.p. 146–148° (with decomposition).

Found %: Sb 21.87, 21.97. $C_{18}H_{14}N_2Cl_5Sb$. Calculated %: Sb 21.85.

h) From 1 g (0.0032 g-mole) of diphenylchlorostibine and 1.11 g (0.0033 g-mole) of the double salt of p-chlorophenyldiazonium chloride and ferric chloride, under the conditions of experiment (a), we obtained 1.3 g of the double salt of P-chlorophenyldiazonium chloride and diphenyl antimony trichloride. Yield 73%. M.p. 151–153° (with decomposition).

Found %: Sb 21.77, 21.87. $C_{18}H_{14}N_2Cl_5Sb$. Calculated %: Sb 21.85.

3. Reaction of diphenylchlorostibine with the double diazonium salts of zinc chloride. a) We dissolved 0.5 g (0.0016 g-mole) of diphenylchlorostibine in 5 ml of glacial acetic acid and added 0.7 g (0.0017 g-mole) of the double salt of phenyldiazonium chloride and zinc chloride dissolved in a mixture of 3 ml of glacial acetic acid and 1.5 ml of concentrated hydrochloric acid. Reaction occurred with evolution of nitrogen. The reaction mixture was cooled. We obtained the double salt of phenyldiazonium chloride and diphenyl antimony trichloride, which was filtered, washed with glacial acetic acid, alcohol, and ether. Yield 0.61 g (73%). M.p. 144–167° (with decomposition).

Found %: Sb 23.10, 23.59. $C_{18}H_{15}N_2Cl_4Sb$. Calculated %: Sb 23.29.

b) From 0.5 g (0.0016 g-mole) of diphenylchlorostibine and 1.44 g (0.0034 g-mole) of the double salt of phenyldiazonium chloride and zinc chloride, under the conditions of the previous experiment we obtained 0.74 g of the double salt of phenyldiazonium chloride and diphenyl antimony trichloride. Yield 88%. M.p. 155–167° (with decomposition).

Found %: Sb 23.21, 23.30. $C_{18}H_{15}N_2Cl_4Sb$. Calculated %: Sb 23.29.

c) One g (0.0032 g-mole) of diphenylchlorostibine was placed in a flask connected to a dropping funnel and an inlet and outlet tube for carbon dioxide. A stream of carbon dioxide displaced the air from the apparatus and then the diphenylchlorostibine was dissolved by adding 20 ml of glacial acetic acid through the funnel. When the diphenylchlorostibine had fully dissolved, we added a solution of 1.44 g (0.0034 g-mole) of the double salt of phenyldiazonium chloride and zinc chloride in an acid mixture of 8 ml of glacial acetic acid and 4 ml of concentrated hydrochloric acid. Formation of the double salt was accompanied by evolution of nitrogen. The contents of the reaction flask were driven over by a stream of carbon dioxide onto a funnel with a filter bottom, the precipitate was washed with glacial acetic acid, alcohol, and ether. Yield 1.3 g (77%). M.p. 148–160° (with decomposition).

Found %: Sb 23.18, 23.21. $C_{18}H_{15}N_2Cl_4Sb$. Calculated %: Sb 23.29.

d) From 1.34 g (0.0043 g-mole) of diphenylchlorostibine and 1.95 g (0.0041 g-mole) of the double salt of p-anisyldiazonium chloride and zinc chloride under the conditions of experiment (a) we obtained 1.9 g of the double dalt of p-anisyldiazonium chloride and diphenylantimony trichloride. Yield 80%. M. p. 152-153° (with decomposition).
known diphenylantimony trichloride gave no depression.

Found %: Sb 22.31, 22.20. $C_{19}H_{17}ON_2Cl_4Sb$. Calculated %: Sb 22.03.

e) From 1 g (0.0032 g-mole) of diphenylchlorostibine and 1.6 g (0.0032 g-mole) of the double salt dimethylaminophenyldiazonium chloride and zinc chloride, under the conditions of experiment (a), we obtained 1.6 g of the double salt of p-dimethylaminophenyldiazonium chloride and diphenyl antimony trichloride. Yield 88%. M.p. 145.5–146.5° (with decomposition).

Found %: Sb 21.65, 21.67. $C_{20}H_{20}N_3Cl_4Sb$. Calculated %: Sb 21.53.

4. Reaction of diphenylchlorostibine with solid phenyldiazonium chloride. One g (0.0032 g-mole) of diphenylchlorostibine was dissolved in the minimum amount of anhydrous methyl alcohol. With ice cooling, we added a solution of 0.45 g (0.0032 g-mole) of solid phenyldiazonium chloride in the minimum amount of anhydrous methyl alcohol. There was a violent evolution of nitrogen and the solution became red. The double salt of phenyldiazonium chloride and diphenyl antimony trichloride which separated was filtered and washed with alcohol and ether. Yield 0.4 g (24% calculated on the diphenylchlorostibine, 71% calculated on the phenyldiazonium chloride). M.p. 152–164° (with decomposition).

Found %: Sb 23.27, 23.52. $C_{18}H_{15}N_2Cl_4Sb$. Calculated %: Sb 23.29.

5. Oxidation of diphenylchlorostibine. a) By oxides of nitrogen. To 2 ml of concentrated hydrochloric acid and 2 g of ice we added a solution of 0.7 g (0.0102 g-mole) of sodium nitrite in 2 ml of water. To the resulting solution we added 10 ml of glacial acetic acid, and with cooling, poured in a solution of 1.75 g (0.0056 g-mole) of diphenylchlorostibine in 20 ml of glacial acetic acid. The reaction mixture was poured into dilute ammonia, the precipitate was filtered off and washed with alcohol and ether. Diphenylstibinic acid was obtained in quantitative yield. Recrystallization from 5 N hydrochloric acid gave diphenyl antimony trichloride with m.p. 172–173°; the literature gives 172–173° [6]. A mixed melting point with known diphenyl antimony trichloride gave no depression.

b) Ferric chloride. One g (0.0032 g-mole) of diphenylchlorostibine was dissolved in 2 ml of alcohol saturated with hydrogen chloride. A solution of 1.5 g (0.0092 g-mole) of ferric chloride in 2 ml of anhydrous acetone was added with cooling with salt and ice. The resulting solution was evaporated. The crystals of diphenyl antimony trichloride which separated were washed with 5 N hydrochloric acid and recrystallized from 5 N hydrochloric acid. Yield 0.75 g (61%). M.p. 173–175°; literature data 175° [10].

c) Oxygen of the air in the presence of zinc chloride. We added 10 ml of glacial acetic acid to 0.5 g (0.0016 g-mole) of diphenylchlorostibine and poured in a solution of 0.22 g (0.0016 g-mole) of zinc chloride in a mixture of 4 ml of glacial acetic acid and 2 ml of concentrated hydrochloric acid. The reaction mixture was hydrolyzed with a 5% ammonia solution with ice. The precipitate was filtered and washed with water, pressed out well, and washed with alcohol and ether; the ether was evaporated and the residue was treated with acetic acid. We obtained 0.29 g of diphenylstibine acetate. Yield 54%. The diphenylstibine acetate was transformed into diphenylchlorostibine with m.p. 65°; the literature gives 68° [11]. The residue which did not dissolve in alcohol and ether was diphenyl stibinic acid. Yield 0.1 g (20%). After recrystallization from 5 N hydrochloric acid it had m.p. 173–175°; the literature gives 175° [10]. A mixed melting point with known diphenylantimony trichloride gave no depression.

SUMMARY

1. We have showed that the reaction of diphenylchlorostibine with aryl diazonium chlorides (free or bound in a complex) results in formation not of the double diazonium salt of diphenylchlorostibine, but of the double diazonium salt of diphenyl antimony trichloride; evidently the double diazonium salt of diphenylchlorostibine, in general, cannot exist under ordinary conditions.

2. We have shown that in the work of A. B. Bruker and N. M. Nikiforova [6] the double diazonium salt of diphenyl antimony trichloride was erroneously taken for the double diazonium salt of diphenylchlorostibine.

LITERATURE CITED

[1] O. A. Reutov, Doklady Akad. Nauk SSSR 87, 73 (1952).

[2] A. N. Nesmeyanov, O. A. Reutov and P. Knol', Izv. Akad. Nauk SSSR, Otd. Khim. Nauk 3, 410 (1954). •

[3] O. A. Reutov, Doklady Akad. Nauk SSSR 87, 991 (1952).

[4] O. A. Reutov and V. V. Kondrat'eva, Zhur. Obshchei Khim. 24, 1259 (1954). •

[5] O. A. Reutov and A. G. Markovskaya, Doklady Akad. Nauk SSSR 99, 543 (1954).

[6] A. B. Bruker and N. M. Nikiforova, Zhur. Obshchei Khim. 18, 1132 (1948).

[7] O. A. Reutov and A. G. Markovskaya, Doklady Akad. Nauk SSSR 98, 979 (1954).

[8] O. A. Reutov, A. G. Markovskaya and A. N. Lovtsova, Doklady Akad. Nauk SSSR 99, 269 (1954).

[9] O. A. Reutov and O. A. Ptitsyna, Doklady Akad. Nauk SSSR 102, 291 (1955).

[10] H. Schmidt, Lieb. Ann. 429, 142 (1922).

[11] K. A. Kocheskov and A. P. Skoldinov, Synthetic Methods in the Field of Metalloorganic compounds of Antimony and Bismuth [in Russian] (1947) p. 95.

•Original Russian pagination. See C. B. translation.

ISOTOPE EXCHANGE OF OXYGEN IN SUBSTITUTED BENZOIC ACIDS WITH H_2O^{18}

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Translated from Zhurnal Ooshchei Khimii, Vol. 29, No. 12, pp. 3895-3897, December, 1959

Original article submitted December 8, 1958

In the present work we have studied the rate of exchange with H_2O^{18} of the oxygen of benzoic acid which contains as substituents in the ortho-, meta-, and para positions the residues $-NO_2$, -Cl, -OH, -SH, and $-NH_2$.

The experiments were carried out in water-alcohol solutions* of about the same concentration without catalysts and in the presence of 0.4 N hydrochloric acid. The substance, water (or acid solution), and alcohol were taken in the ratio 0.002: 0.02: 0.006 mole; heating was carried out in a sealed ampule of Jena glass, the surface of which was first treated by boiling with hydrochloric acid. After exchange, the substance was separated from water and alcohol and purified by sublimation in a vacuum. Its purity was controlled by its melting point. Isotopic analysis was carried out by the method which one of us had developed [1], which consisted in cracking and heating in a quartz ampule at 750° of a sample of the substance studied and a given amount of CO_2 of normal isotopic composition, with later mass spectrometric analysis of the CO_2, which had reached an equilibrium distribution of the O^{18} from the cracking products. The heavy oxygen water for the experiments was purified by heating with acid and then with alkali solutions of potassium permanganate, redistilling four times in a quartz apparatus, and

TABLE

Rate of Exchange of O^{18} and Dissociation Constants of the Substituted Benzoic Acids

Name of acid	Rate const. in hr^{-1} at 170° without adding HCl	Rate const. in hr^{-1} in presence of 0.4 N HCl	Dissociation const. [2]
Benzoic	0.083	0.55 (110°)	$6.46 \cdot 10^{-5}$ (25°)
o-Chlorobenzoic	0.16	0.19 (110)	$1.20 \cdot 10^{-3}$ (25)
m-Chlorobenzoic	0.19	0.46 (110)	$1.51 \cdot 10^{-4}$ (25)
p-Chlorobenzoic	0.13	0.050 (110)	$1.04 \cdot 10^{-4}$ (25)
o-Nitrobenzoic	0.18	0.39 (150)	$6.95 \cdot 10^{-3}$ (18)
m-Nitrobenzoic	0.39	—	$3.40 \cdot 10^{-4}$ (25)
p-Nitrobenzoic	0.78	0.33 (110)	$3.93 \cdot 10^{-4}$ (25)
o-Hydroxybenzoic	—	0.18 (110)	$1.07 \cdot 10^{-3}$ (19)
m-Hydroxybenzoic	0.28	1.15 (110)	$8.7 \cdot 10^{-5}$ (19)
p-Hydroxybenzoic	—	0.54 (110)	$3.3 \cdot 10^{-5}$ (19)
o-Aminobenzoic	No exchange after 3 hrs	No exchange after 3 hrs (100°)	$1.07 \cdot 10^{-7}$ (25)
m-Aminobenzoic	—	0.11 (150)	$1.67 \cdot 10^{-5}$ (25)
p-Aminobenzoic	No exchange after 10 hrs	No exchange after 15 hrs (150)	$1.2 \cdot 10^{-5}$ (25)
Thiosalicylic	0.075	0.46 (150)	—
o-$HOOCC_6H_4NH_2 \cdot HCl$	37% exchange after 3 hrs at 100°		
o-$KOOC—C_6H_4—NH_2$	58% exchange after 3 hrs at 170° in 60% aqueous potassium hydroxide solution; no exchange without adding alkali		

*We found that under the conditions of the experiments alcohol did not take part in the exchange.

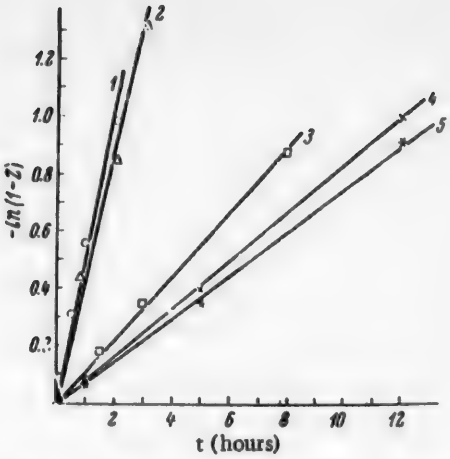


Fig. 1. Exchange rate of benzoic, m-aminobenzoic, and thiosalicylic acids. In the presence of 0.4 N H Cl: 1) benzoic at 110°; 2) thiosalicylic at 150°; 3) m-aminobenzoic at 150°. In the absence of HCl: 4) benzoic at 170°; 5) thiosalicylic at 170°.

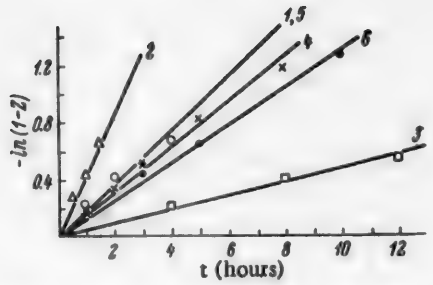


Fig. 2. Exchange rate of chlorobenzoic acids. In the presence of 0.4 N HCl at 110°: 1) o-chlorobenzoic; 2) m-clorobenzoic; 3) p-chlorobenzoic. In the absence of HCl at 170°: 4) o-chlorobenzoic; 5- m-chlorobenzoic; 6) p-chlorobenzoic.

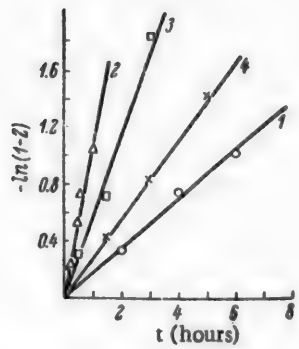


Fig. 3. Exchange rate of hydroxybenzoic acids. In the presence of 0.4 N H Cl at 110°: 1) o-hydroxybenzoic; 2) m-hydroxybenzoic; 3) p-hydroxybenzoic. In the absence of H Cl at 170°: 4) m-hydroxybenzoic.

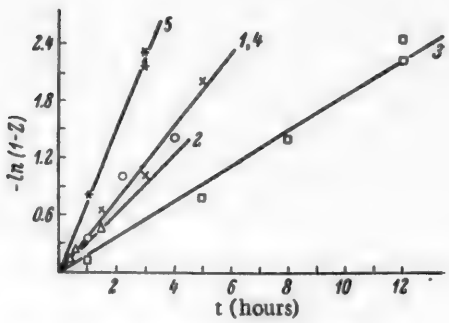
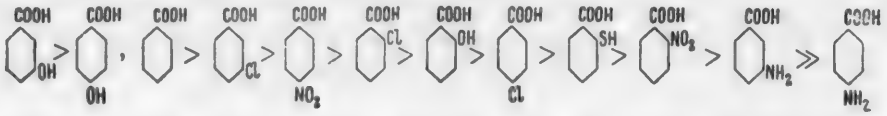


Fig. 4. Exchange rate of nitrobenzoic acids. In the presence of 0.4 N HCl: 1) o-nitrobenzoic at 150°; 2) p-nitrobenzoic at 110°. In the absence of HCl at 170°: 3) o-nitrobenzoic; 4) m-nitrobenzoic; 5) p-nitrobenzoic.

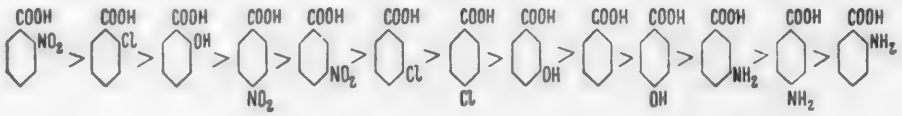
keeping in a quartz vessel.

The results are given in Fig. 1-4 in the form of the relation of the value of ln (1-Z) (where Z is the amount of exchange) to time t. As the figures show, the experimental points fall satisfactorily on a straight line, which corresponds to a kinetic equation of the first order. In the table we give the rate constants found from this straight line for the exchange as compared to the dissociation constants of the acids studied, and also our qualitative data on the exchange of salts of o-aminobenzoic acid.

The results show that hydrochloric acid hastens exchange considerably. The substances studied can be arranged in the following order as to rate of exchange in the presence of hydrochloric acid:



this directly reflects the relation of exchange rate to structure since the addition of hydrochloric acid assures a constant pH in spite of the different strengths of the organic acids and removes the effect of differences in acidity on the rate. This series does not show a clear relation between the electrical properties and positive substituents with the nature of their effect on exchange in substituted benzoic acids. Comparison with the arrangement of these substances according to acidity:



does not show a regularity between exchange rate and acid strength.

One of us has encountered similar difficulties in earlier work in explaining experimental data [3]. This shows that for an understanding of the relation of reaction rate to structure even in the simplest case of isotopic exchange there must be a much greater accumulation of experimental material. The present work is one of the first attempts to study the relation of exchange rate of carboxylic acids to the nature and position of substituents. Except for some fragmentary data [4,5] there is only one study in the literature [5] in which there is an attempt like ours to set up the problem, and the experimental material is slight. The authors of this work also did not find a clear relation between rate of exchange and nature of substituents.

SUMMARY

We have studied the kinetics of isotopic exchange of oxygen with benzoic acids which contain substituents in the ortho-, meta-, and para-positions using H_2O^{18}. The exchange reaction is catalyzed by hydrochloric acid. We did not find a clear relation between nature and position of the substituents and their effect on the exchange, nor a relation between rate of exchange and acid strength.

LITERATURE CITED

[1] I. P. Gragerov, Problems of Kinetics and Catalysis, IX. "Isotopes in catalysis". [In Russian] (1957) p. 373.

[2] Handbook of Chemistry [in Russian] 3, 495 (1952).

[3] V. V. Fesenko and I. P. Gragerov, Doklady Akad. Nauk SSSR 101, 695 (1955).

[4] M. Cohn and H. Urey, J. Am. Chem. Soc. 60, 679 (1938); J. Chem. Phys. 6, 175 (1938).

[5] M. Koizumi and T. Titani, Bull. Chem. Soc. Japan 13, 463, 607 (1938).

[6] M. L. Bender, R. R. Stone, and R. S. Dewey, J. Am. Chem. Soc. 78, 319 (1956).

THE "PERI EFFECT" AND ABSORPTION SPECTRA OF SOME SOME SUBSTITUTED S-(1-NAPHTHYL)-THIOGLYCOLIC ACIDS

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3898-3901, December, 1959

Original article submitted December 23, 1958

The reciprocal effect of atoms occurring in the peri-position of the naphthalene ring has been little studied. The literature on absorption spectra of peri-derivatives of naphthalene is also scanty.

Since the distance between the peri-atoms of carbon in the naphthalene ring is 2.46 A, most atom substituents in the peri-position are found at distances less than the sum of their van der Waals radii. Thus, for the case of oxygen and sulfur, the sum of these radii is 1.85 A + 1.38 = 3.23 A, which considerably surpasses the above distance between the peri-positions of the naphthalene ring.

Such an unusually close mutual relation of two atoms which are not covalently bound will obviously result in an overlapping of the outer electron shells of both atoms. The molecule then will form a supplementary system of electron interactions; such a system should affect the absorption spectrum of the substance similar to an increase of the conjugated chain, that is, it should deepen the color ("peri-effect").

Clar and Marschalk [1] thus explained the unusually deep color of 5,6,11,12-tetrachlorotetracene and tetracene tetrasulfide; they also considered the absorption spectra of 1,4- and 1,5-dichloronaphthalenes. However, in the work of these authors it was not shown that the peri-derivatives of naphthalene were more deeply colored than the 1,4- and 1,5-isomers.

In the present work we have planned to show the presence of the "peri-effect" in a series of peri-substituted S-(1-naphthyl)thioglycolic acids by comparing the absorption spectra of these compounds with the absorption spectra of the corresponding 1,4- and 1,5-isomers and also to establish a relation between the number of free electrons in the outer shell of the atom substituents and the size of the resulting "peri-effect" in these atoms.

We chose the series of S-(1-naphthyl)thioglycolic acids because the napthalene analogs of the thioindigo dyes are genetically related to the series.

We determined the absorption spectra (in 95% ethanol) of S-(1-naphthyl)-thioglycolic acid and its 4-methoxy, 5-methoxy, 8-methoxy, 4-chloro, 5-chloro, 8-chloro, 5-bromo, 8-bromo, and 8-carboxy derivatives.

The results of these experiments are given in the table; the figure gives the absorption spectrum of S-(1-naphthyl)thioglycolic acid, typical for the above mentioned derivatives of this acid.

From a consideration of the data of the table we can draw the following conclusions.

1. In the series of 1,4-, 1,5-, and 1,8-methoxynaphthylthioglycolic acids, just as in the series of chloronaphthylthioglycolic acids and the two bromonaphthylthioglycolic acids, the 1,8-isomer has its maximum absorption at the greatest wave length. The coefficient of molecular extinction for the 1,8-isomer is also at the greatest. This shows that in the three series which we have discussed there is a "peri-effect", that is, a deepening of color (in the ultraviolet) of the 1,8-isomer, probably because of the mutual penetration of the electron shells of both atoms.

2. We estimated the size of the "peri-effect" by the difference between the absorption maximum of the wave length of the 1,8- and the 1,5-isomers; this obviously increases with increase in the number of unbound

Characteristics of Absorption Spectra of Derivatives of S-(1-naphthyl)-thioglycolic Acid

Thioglycolic acid	λ max (mμ)	λ min (mμ)	$E_{max} \cdot 10^{-3}$
S-(1-naphthyl)	303	265	6.5
S-(1-naphthyl-8-carboxy)	303	265	5.5
S-(1-naphthyl-5-chloro)	312.5	267.5	7.3
S-(1-naphthyl-4-chloro)	315	272	8.2
S-(1-naphthyl-8-chloro)	327	275	8.4
S-(1-naphthyl-5-methoxy)	307.5	257.5	9.8
S-(1-naphthyl-4-methoxy)	308	267.5	9.6
S-(1-naphthyl-8-methoxy)	313.5	272.5	10.7
S-(1-naphthyl-5-bromo)	315	272.5	7.8
S-(1-naphthyl-8-bromo)	327	282.5	7.9

electrons in the outer electron shell of the substituent atoms. Actually, the carbon atom of the carboxyl group in the 1,8-carboxynaphthylthioglycolic acid does not have any unbound electrons. Here the "peri-effect" is not found (this compound absorbs at the same wave length as the unsubstituted acid; the coefficient of extinction is greatly lowered). The oxygen atom of the methoxy group has four unbound electrons in the outer electron shell; the "peri-effect" in 1,8-methoxynaphthylthioglycolic acid is 6 mμ. The chlorine and bromine atoms have six outer unbound electrons. Corresponding to this, the "peri-effect" in these compounds is still greater (14.5 mμ).

Our viewpoint explains the results given in the literature. Thus, of the 1,4-, 1,5-, and 1,8-dichloronaphthalenes, the latter has the deepest color in the ultraviolet and shows the greatest coefficient of molecular extinction (presence of "peri-effect") [2], and, on the contrary, in the 1,4-, 1,5-, and 1,8-dimethylnaphthalenes the peri-isomer is least deeply colored in the ultraviolet and has the minimum coefficient of molecular extinction [3]; there is no "peri-effect" in view of the absence of unbound electrons in the methyl group.

3. The coefficients of molecular extinction of the peri-isomers are decreased in the series of substituents $Br < Cl < OCH_3$. Since the volumes increase in the same order (oxygen of the methoxy group < chlorine < bromine), this suggests that increased volume of the substituent atom decreases the coefficient of molecular extinction.

EXPERIMENTAL

S-(1-naphthyl)thioglycolic acid was prepared from α-naphthylamine by the method described earlier by one of us [4].

S-(1-naphthyl-8-chloro)thioglycolic acid was obtained from the technical product by recrystallization from chlorobenzene; m.p. 160–161°.

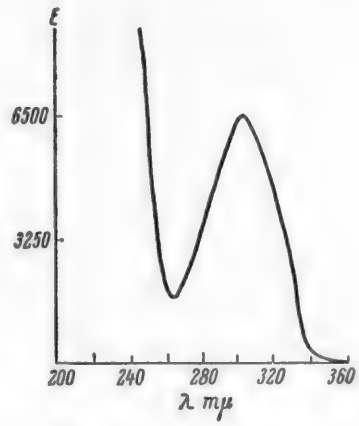
S-(1-naphthyl-4-chloro)thioglycolic acid was obtained from 4-aminonaphthalene-1-sulfonic acid. 4-Chloronaphthalene-1-sulfonyl chloride, obtained from the sodium salt of the sulfonic acid and phosphorus pentachloride, was reduced by zinc and sulfuric acid to the corresponding thiol which was then condensed with monochloroacetic acid. Colorless crystals (from a large amount of water); m.p. 127.5–128.5°.

Found %: S 12.7. $C_{12}H_9O_2SCl$. Calculated %: S 12.7.

S-(1-naphthyl-5-chloro)thioglycolic acid was obtained in the same way as the preceding isomer from 5-aminonaphthalene-1-sulfonic acid. Colorless crystals (from a large amount of water); m.p. 157–157.8°.

Found %: Cl 14.0; S 12.5. $C_{12}H_9O_2SCl$. Calculated %: Cl 14.0; S 12.7.

S-(1-naphthyl-5-bromo)thioglycolic acid was also obtained from 5-aminonaphthalene-1-sulfonic acid. Colorless crystals (from a large



Absorption spectrum of S-(1-naphthyl)thioglycolic acid.

amount of water); m.p. 233–234°.

Found %: Br 26.7. $C_{12}H_9O_2SBr$. Calculated %: Br 26.9.

S-(1-naphthyl-8-bromo)thioglycolic acid was synthesized through S-(1-naphthyl-8-amino)thioglycolic acid; the latter was obtained by mixing together at 14–16° an alkaline solution of sodium monochloroacetate with 1,8-aminonaphthalenethiol chlorostannate which had been described previously [5]; the sodium S-(1-naphthyl-8-amino) thioglycolate was easily salted out, and by substitution of the diazo group in this acid with bromine we obtained S-(1-naphthyl-8-bromo)-thioglycolic acid, colorless crystals (from chlorobenzene); m.p. 137.5–138.5°.

Found %: C 48.9; H 3.3; Br 27.3. $C_{12}H_9O_2SBr$. Calculated %: C 48.5; H 3.1; Br 26.9.

S-(1-naphthyl-4-methoxy)thioglycolic acid was synthesized from 1,4-naphthol sulfonic acid. Methylation of the sodium salt of this acid was carried out in an alkaline medium with dimethyl sulfate at 80–90°. When sodium 1,4-methoxynapthalenesulfonate was treated with phosphorus pentachloride, we obtained 1,4-methoxynaphthalene-sulfonyl chloride. Crystals (from benzene); m.p. 96–97°.

Found %: S 12.3. $C_{11}H_9O_3SCl$. Calculated %: S 12.5.

Reduction of this compound with zinc and sulfuric acid and later condensation of the resulting thiol with monochloroacetic acid gave S-(1-naphthyl-4-methoxy)thioglycolic acid. Colorless crystals (from water); m.p. 115–116°.

Found %: S 12.9. $C_{13}H_{12}O_3S$. Calculated %: S 12.9.

S-(1-naphthyl-5-methoxy)thioglycolic acid was obtained from 1,5-naphthol sulfonic acid in the same way as the above described 1,4-isomer. Colorless crystals (from a large amount of water); m.p. 160.5–161.5°.

Found %: S 12.8. $C_{13}H_{12}O_3S$. Calculated %: S 12.9.

S-(1-naphthyl-8-methoxy)thioglycolic acid was synthesized from naphthosulfone by boiling the latter for several hours with an excess of an aqueous solution of potassium hydroxide. The resulting solution of potassium 1,8-naphtholate sulfonate was treated with dimethyl sulfate as described above for the 1,4-isomer. From potassium 1,8-methoxynaphthalene sulfonate in the usual way (see above) we obtained S-(1-naphthyl-8-methoxy)thioglycolic acid, colorless crystals (from water); m.p. 137.5–138°.

Found %: C 62.7; S 13.0. $C_{13}H_{12}O_3S$. Calculated %: C 62.9; S 12.9.

S-(1-naphthyl-8-carboxy)thioglycolic acid was obtained by the known method [6].

The absorption spectra of the above acids (see table) were determined on an SF-4 spectrophotometer.

SUMMARY

We have determined the absorption spectra of S-(1-naphthyl)thioglycolic acid and some of its derivatives. We have found that in 1,4-, 1,5-, and 1,8-halogen (or methoxy) naphthylthioglycolic acids, the "peri-isomers" have the deepest color and the greatest coefficient of molecular extinction. We have given an explanation of this effect (the "peri-effect") based on the possibility of mutual penetration of unbound electrons of the outer electron shell of the atoms in the peri-position. We have found that the "peri-effect" increases with increased number of unbound electrons in the outer shell of the substituent atom.

LITERATURE CITED

[1] E. Clar and C. Marschalk, Bull. Soc. Chim. 433 (1950); C. A. 1571 (1951).

[2] L.-B. T., II Erg. 680.

[3] W. Mosby, J. Am. Chem. Soc. 75, 3348 (1953).

[4] G. M. Oksengendler and Yu. E. Gerasimenko, Zhur. Obshchei Khim. 27, 3214 (1957).*

[5] M. T. Bogert and J. H. Bartlett, J. Am. Chem. Soc. 53, 4076 (1931).

[6] P. Friedländer and N. Woroshzow, Ann. Chim. 388, 1 (1912).

*Original Russian pagination. See C. B. translation.

THE REACTION OF 1-NAPHTHYLMAGNESIUM BROMIDE WITH ESTERS OF MONOCARBOXYLIC ACIDS

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3901-3908, December, 1959

Original article submitted December 8, 1958

Until the present time, more or less complete studies have been made only of the reaction of 1-naphthylmagnesium halides with ethyl formate. It has been found that in the case of a three-fold excess of ethyl formate in the cold (-50°) there is formed mainly 1-naphthoic aldehyde [1], while, on the contrary, the use of 2.5—3 times excess of halide at positive temperatures results in the formation of di- (1-naphthyl)carbinol with a yield of 80% or better [2-4]. At equimolar ratios of the reagents the reaction goes in part anomalously [5] and along with dinaphthylcarbinol there is formed the ethyl ether corresponding to it, (yield up to 22%), and, probably, symmetrical tetra-(1-naphthyl)ethane. There was also a very superficial study of the reaction of this Grignard reagent with esters of high molecular weight acids, montanic [6] and stearic [7]. The ethyl ester of the first gave the corresponding tertiary alcohol, di-(1-naphthyl)-heptacosylcarbinol, while the methyl ester of the second gave heptadecyl-1-naphthyl ketone. The formation of the corresponding 1-naphthyl ketone was also observed in the condensation of 1-naphthylmagnesium bromide with methyl diphenylhydroxyacetate [8] and ethyl hydrocinnamate [9], carvacryl acetate [10] and monochloroacetate [11], while with ethyl acetate [12] and ethyl α-hydroxyisobutyrate [13], 1-naphthylmagnesium bromide reacts with formation of the corresponding tertiary alcohol. Finally, from the reaction products of 1-$C_{10}H_7MgBr$ with ethyl laurate the ketone was also isolated (lauro-1-naphthone), and the tertiary alcohol di-(1-naphthyl)undecylcarbinol [14]. Thus, the literature data on the condensation of 1-naphthylmagnesium bromide with esters is very scattered and contradictory.

In order to fill this gap, we carried out a systematic study of the reactions of 1-naphthylmagnesium bromide with esters of normal monocarboxylic acids from acetic to caprylic, inclusive. In all cases we isolated as the main reaction product the corresponding alkyl 1-naphthyl ketone and 1',1'-di(1-naphthyl)-1'-alkene, the product of dehydration of the corresponding tertiary alcohol. The formation along with the dinaphthylalkenes of the products of incomplete occurrence of the Grignard reaction, the corresponding alkyl naphthyl ketones, can be explained by the presence of known spatial difficulties in the 1-naphthyl radical, the second ring of which can be regarded as an ortho-substituent [11]. Actually, when we use a spatially simple reagent with the same C_{10} as naphthyl, n-decylmagnesium bromide in the Grignard reaction with ethyl acetate, we do not succeed in getting methyl n-decyl ketone even under the optimum conditions for obtaining the alkyl naphthyl ketones; the only reaction product is the tertiary alcohol, methyl di-n-decylcarbinol (yield 61%). In the same way, phenylmagnesium bromide [6,7,15] and biphenylmagnesium bromide [16], which also have no spatial difficulties, react with esters of monocarboxylic acids with formation merely of tertiary alcohols and the products of their dehydration.

We also found that the yield of the chief product in the reaction studied depended mainly on the ratio of the starting reagents and the value of the dissociation constants of the acids whose esters were used in the reaction, and to a lesser degree on the nature of the alkoxyl groups of the ester used and the conditions of carrying out the reaction. As the results in Table 1 show, the use in the reaction of an excess of Grignard reagent, that is, increasing the ratio of 1-$C_{10}H_7Br$ to ester, permits formation of the corresponding alkyl 1-naphthyl ketone, and not the dinaphthylalkylcarbinol (dinaphthylalkene), as would be expected.

TABLE 1

Mole ratio of 1-$C_{10}H_7Br$ to $CH_3COOC_2H_5$ *	Yield of reaction products (in %) **	
	methyl 1-naphthyl ketone	1',1'-dinaphthylethylene
1 : 2	9	52
1 : 1.5	8.4	46
1 : 1	7.7	54.5
1.5 : 1	15	47
2 : 1	29	39
2.3 : 1	32	47
3 : 1	46	28
4 : 1	51	24

* "Direct" addition of the components at the boiling point of ether followed by stirring 8-10 hr at 35°.

** Yield of crude product calculated on the starting reagent (in deficient amount).

It is interesting to observe that replacing 1-$C_{10}H_7MgBr$ by the more reactive 1-napthyl lithium in excess (ratio of 1-$C_{10}H_7Cl$: $CH_3COOC_2H_5$ 4:1 or 5:1), under the conditions used, acutally does not change the ratio of the reaction products: the yield of crude methyl naphthyl ketone is 30—40%, of dinaphthylethylene, 70—40%.

The nature of the alkoxyl group of the ester acts on the results of the reaction to a much smaller degree than the ratio of reagents. Thus, in the condensation of 1-naphthylmagnesium bromide with various esters of acetic acid (from methyl to n-butyl inclusive) under the same conditions (mole ratio 1-$C_{10}H_7Br$: CH_3COOR = 2.5:1), the yield of methyl 1-naphthyl ketone varies from 34—45% and of 1', 1'-dinaphthylethane from 46 to 38%, which can be partly explained by experimental errors. In the case of a constant alkoxyl group in the ester and conditions of carrying out the reaction, the yield of products depends only on the nature of the acid whose ester takes part in the reaction, and as we showed, the yield of alkyl 1-naphthyl ketones increases as the dissociation constants of the acids decrease (Table 2). From ethyl formate (for HCOOH at 25°, $K = 21.4 \cdot 10^{-5}$), as would be expected, under analogous conditions 1-$C_{10}H_7CHO$ is generally not formed at all.

TABLE 2

Significance of R in $RCOOC_2H_5$ *	Dissociation const. of RCCOOH at 25° according to [17], $K \cdot 10^{-5}$	Yield of reaction product, %	
		1-$C_{10}H_7$—C(=O)—R	$(1\text{-}C_{10}H_7)_2C{=}CHR''$
CH_3	1.82	34	46
C_2H_5	1.31	75	24
n-C_3H_7	1.48	40	43
n-C_5H_{11}	1.45	41	51
n-C_6H_{13}	1.42	42	50
n-C_7H_{15}	1.43	45	32

* Mole ratio 1-$C_{10}H_7Br$ to $RCOOC_2H_5$ 2.5:1. Conditions of running the experiment, see Table 1. R=R"CH_2.

We also established the effect on the final result of the conditions of running the reaction of 1-naphthylmagnesium bromide and ethyl acetate (we ran about 30 experiments); such conditions as temperature, duration, order of adding reagents, etc. Other conditions being equal, the rate and order of adding the reagents, "directly" (ester to Grignard reagent) or "inversely" (Grignard reagent to ester), had almost no effect on yield of reaction products.

The temperature and duration of the reaction after mixing had a definite effect on the results of the reaction, and the nature of this effect depended to a considerable extent on the mole ratio of the starting components. Thus, in the case of using a 1.5-fold excess of ethyl acetate, decreasing the reaction temperature from 35° to (-10 to -40°), and at the same time shortening the duration of the experiment from 10—12 hours to 0.52 hours increased the content, in the product, of methyl 1-naphthyl ketone 2.5—3.5 times (from 7—8 to 20—27%) with almost unchanged total yield of reaction product (55—70%). When we used 1-naphthyl bromide and ethyl acetate in the mole ratios 1:1 and 1.5:1, lowering the temperature (from 35° to 0 to -10°) and decreasing the duration of the reaction caused an increased yield of methyl naphthyl ketone of only 1.5—2 times (from 8—15 to 17—24%), and in the case of a greater excess of 1-$C_{10}H_7MgBr$ (1-$C_{10}H_7Br$: $CH_3COOC_2H_5 \geq 2$ on the contrary, a marked fall in yield of ketone (from 40—50 to 26—18%) and also in total yield of products of the Grignard reaction, as is seen from the data of Table 3. However, we should say that at very low temperatures (-60° or below), the reaction even in the case of 1.5-fold excess of ethyl acetate goes very slowly and incompletely, though toward preferential formation of ketone (yield of methyl naphthyl ketone 16%, of dinaphthylethylene, 4.5%).

Starting from our results and those given in the literature [11, 18—20], the following is the most probable mechanism of the Grignard reaction which we study (in simplest form).

TABLE 3

Mole ratio, 1-$C_{10}H_7Br$ to ethyl acetate*	Reaction temperature	Time of stirring after addition of ethyl acetate, min	Yield of reaction products, %	
			methyl naphthyl ketone	dinaphthylethylene
1 : 1.5	35°	600	7—8	46—50
1 : 1.5	~15	60	13	47
1 : 1.5	~ 0	120	16	60
3 : 1	35	600	46	28
3 : 1	20—25	30	38	25
3 : 1	5	5	26	52
4 : 1	35	600	51	24
4 : 1	5	15	18	36

* "Direct" order of mixing reagents. Amount of starting ethyl acetate 0.2 mole; time of its addition, 90 minutes.

In the case of excess Grignard reagent (1-$C_{10}H_7Br$: RCOOR' ≥ 2 : 1) the binding of the first molecule of 1-$C_{10}H_7MgBr$ to the ester will occur most rapidly on the carbonyl bond.

$$RCOOR' + 1\text{-}C_{10}H_7MgBr \longrightarrow R{-}C(1\text{-}C_{10}H_7)(O{-}R')(O{-}MgBr)$$

(I)

Increasing the excess of Grignard reagent used permits, by the law of mass action, the overcoming of spatial difficulties and the formation of compound (I) in higher yield. Moreover, compound (I) can react with a second molecule of 1-$C_{10}H_7MgBr$ with formation, after hydrolysis, of the tertiary alcohol (II) or, in the case of dehydration, the corresponding olefin (III).

$$(I) + 1\text{-}C_{10}H_7MgBr \longrightarrow R{-}C(1\text{-}C_{10}H_7)_2(O{-}MgBr) \longrightarrow$$

$$\xrightarrow{HOH} R{-}C(OH)(1\text{-}C_{10}H_7)_2 \quad (II) \xrightarrow{-H_2O} R''{-}CH{=}C(1\text{-}C_{10}H_7)_2 \quad (III)$$

However, because of the presence of spatial difficulties in the 1-naphthylradical, the reaction of combining a second molecule of 1-$C_{10}H_7MgBr$ with compound (I) will evidently occur with more difficulty and with much less speed as compared to the reaction of formation of (I), and with hydrolysis of the reaction mixture, unchanged compound (I) will split with the formation of the corresponding ketone (IV), probably according to the scheme:

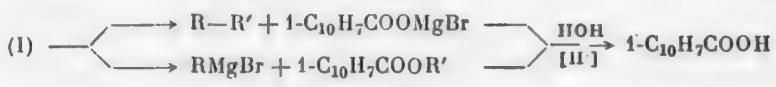
$$(I) + 2HOH \longrightarrow \left[R{-}C(HO)(OH){-}(1\text{-}C_{10}H_7)\right] \xrightarrow{-H_2O} R{-}C(=O){-}(1\text{-}C_{10}H_7) \quad (IV)$$

In view of the different reaction rates of formation of (I) and (II), increase in duration and temperature of the experiment will permit formation of compound (I) in much greater degree than its transformation into compound (II), which is naturally shown in the more rapid relative increase in yield of alkyl 1-naphthyl ketone over dinaphthylalkene (Table 3).

However, the possibility of partial occurrence of this reaction is not excluded, especially with use of excess ester and low temperature and after the stage of intermediate formation of free alkyl naphthyl ketones, in favor of

which, for example, is the considerable increase in yield of methylnaphthyl ketone in experiments with 1.5-fold excess of ethyl acetate at lower temperatures (to -30 to -40°) and shorter reaction duration (Table 3). In the case of excess 1-$C_{10}H_7MgBr$ and positive temperatures, synthesis by this scheme (if it occurs) can be considered only as a method of forming compound (III), that is dinaphthylalkenes, since free alkyl 1-naphthyl ketones [21] and even di-(1-naphthyl)ketone [22] are fully reactive and easily condense with different alkyl and aryl magnesium halides, including 1-$C_{10}H_7MgBr$.

The formation in all the experiments of small amounts (0.5—1.5%) of 1-naphthoic acid can be explained by analogy with the explanation given by Zook [23] for the formation of n-valeric acid in the reaction of CF_3COOLi with n-C_4H_9Li, a partial occurrence of the following reaction.



The explanation of the effect of the dissociation constants of the acids which form the starting esters, and of the nature of the alkoxyl group of the esters on the character and yield of the products formed, is similar to the case of the reaction of 1-$C_{10}H_7MgBr$ with esters of oxalic and chloroacetic acids in the work of Lapkin [11].

EXPERIMENTAL

The starting esters of the n-monocarboxylic acids were either isolated from technical products or obtained by boiling the corresponding carboxylic acid with a two-to three-fold excess of the anhydrous carbinol in the presence of concentrated H_2SO_4. As the solvent for obtaining 1-naphthylmagnesium bromide we used absolute diethyl ether or a mixture of the latter with dry benzene in volume ratio 2:1. When we used the ether-benzene mixture the yield of 1-$C_{10}H_7MgBr$ was higher and reached about 95% because of the better solubility of the latter in the solvent*.

1. Reaction of 1-naphthylmagnesium bromide with ethyl acetate. To 12.2 g (0.5 g-atom) of magnesium in 150 ml of ether was added 83 g (0.4 mole) of 1-naphthyl bromide in 150 ml of ether (about 35°, 2—3 hours). After 1 hour mixing, the Grignard reagent was treated with a solution of 48.2 g (0.6 mole) of ethyl acetate in 150 ml of ether over 15—90 min. The mixture was stirred for 5—600 min more and treated with 5% HCl. The reaction products were fractionated in a vacuum after distilling off the ether. In this way we ran the experiments on condensation of 1-$C_{10}H_7MgBr$ with ethyl acetate at other mole ratios of reagents. The results of these experiments were partly given in the general part of the paper and in Tables 1 and 3. With "inverse" order of adding the reagents (1-$C_{10}H_7MgBr$ to ethyl acetate) the preparation, transfer, and addition of Grignard reagent were carried out in an atomosphere of dry nitrogen. More complete data on study of the reaction of 1-$C_{10}H_7MgBr$ with ethyl acetate is given in the dissertation of one of us [25].

2. Reaction of 1-naphthyl lithium with ethyl acetate. To 15.5 g (2.2 g-atom) of small pieces of lithium in 150 ml of ether, in an atmosphere of nitrogen, we added at 15—20°, over 4.5 hours, 162.6 g (1.0 mole) of 1-chloronaphthalene in 250 ml of ether; half an hour after ending the addition of chloride, we added to the resulting 1-naphthyl lithium, over a period of 2 hours, a solution of 18 g (0.2 mole) of ethyl acetate in 50 ml of ether. The contents of the flask were stirred for another 0.5 hours at room temperature and 10 hours at 35—37°. After the usual treatment of vacuum distillation, we isolated 13.3 g (40%) of crude methyl 1-naphthyl ketone and 45 g (39%) of 1', 1'-dinaphthylethylene. In another experiment, the yield of ketone was 29%, and of dinaphthylethylene, 69.5%.

3. Condensation of esters of n-monocarboxylic acids with excess 1-naphthylmagnesium bromide (mole ratio, 1-$C_{10}H_7Br$: RCOOR′ = 2.5:1). To the Grignard reagent obtained from 207 g (1.0 mole) of 1-bromonaphthalene and 26.8 g (1.1 g-atom) of magnesium in 400 ml of ether, we added, over a period of 1.5—2 hours, a solution of 0.4 mole of the ester in 100—200 ml of ether. Then the contents of the flask were stirred for 1 hour without heating and 8—12 hours at the temperature of boiling ether. After the usual treatment, the reaction products were fractionated in a vacuum. The results of the experiments are given in Table 2.

Increasing the duration of stirring the reaction mixture above 8—12 hours (usually at the boiling temperature) caused considerable tarring and condensation of the reaction products. For example, in the case of ethyl acetate,

*The yield was determined by carbonization of a sample of 1-$C_{10}H_7MgBr$ by solid carbon dioxide, and also by titration during to Gilman [24].

increasing the time of boiling the reaction mixture to 20 hours lowered the yield of methyl naphthyl ketone from 34 to 15%, with simultaneous decrease in yield of dinaphthylethylene from 46 to 39%.

Wide fractions of crude alkyl 1-naphthyl ketones, which from data of oxime formation [26] contained an average of 55–70% ketone, were combined with the corresponding fractions of these ketones from other experiments and twice redistilled in a vacuum, after which their content of ketone rose to 70–90%. These alkyl 1-naphthyl ketones easily formed 2,4-dinitrophenylhydrazones and semicarbazones, which were purified by recrystallization from ethanol or its mixture with ethyl acetate (2–4 times). The melting points of these derivatives, most of which have not been described in the literature, are given in Table 4.

TABLE 4

Significance in R in $1\text{-}C_{10}H_7\text{—}C(=O)\text{—}R$*	2,4-Dinitrophenylhydrazones			Semicarbazones		
	melting point	% N found	% N calculated	melting point	% N found	% N calculated
CH_3	195 —196°	15.90, 15.81	15.99	227 —229°	18.65, 18.73	18.49
C_2H_5	136 —137	15.39, 15.47	15.40	183 —184	17.60, 17.50	17.42
n-C_3H_7	133.5—134.5	15.13, 14.97	14.81	179.5—180.5	16.40, 16.29	16.46
n-C_5H_{11}	151 —152	13.85, 13.98	13.78	210 —211	14.96, 14.84	14.83
n-C_6H_{13}	145 —146	13.01, 12.87	13.32	164 —165.5	14.22, 14.09	14.13

*The properties of these ketones, synthesized by the reation of $1\text{-}C_{10}H_7CN$ and the corresponding $RMgX$, are given in the literature [27, 28].

The 1', 1'-di-(1-naphthyl)-1'-alkenes, isolated by vacuum distillation, were clear yellow resins, most of which crystallized on contact with solvents and on standing. After 3–5 recrystallizations from alcohol, ether, or alcohol-ether mixtures, the dinaphthylalkenes were white crystals with definite melting points. Their properties and elementary analyses are given in Table 5.

TABLE 5

ТАБЛИЦА 5

Significance of "R" in the dinaphthylethenes $(1\text{-}C_{10}H_7)_2C{=}CH\text{—}R''$	Boiling point (pressure in mm)	Melting point	Found % C	Found % H	Empirical formula	Calculated % C	Calculated % H
H *	221—223° (3)	108° **	94.19, 94.30	5.79, 5.78	$C_{22}H_{16}$	94.25	5.75
CH_3	250—253 (4.5)	122	93.94, 93.63	6.14, 6.18	$C_{23}H_{18}$	93.84	6.16
C_2H_5	249—250 (6.5)	100.5	93.41, 93.44	6.62, 6.50	$C_{24}H_{20}$	93.46	6.54
n-C_4H_9	243—244 (3.5)	81	92.80, 92.68	7.11, 7.19	$C_{26}H_{24}$	92.81	7.19
n-C_5H_{11}	230—231 (2)	—	92.77, 92.72	7.41, 7.30	$C_{27}H_{26}$	92.52	7.48
n-C_6H_{13}	233—234 (1)	—	92.32, 92.38	7.84, 7.81	$C_{28}H_{28}$	92.26	7.74

*Picrate-yellow leaflets from 96% alcohol, m.p. 108-108.5° (decomposition).

**According to [12], m.p. 107°.

Besides the alkyl naphthyl ketones and dinaphthylalkenes, in all the experiments we obtained naphthalene and a solid, tarry residue, and also small amounts of crystals, which in a number of cases precipitated as needles in alkyl naphthyl ketone fraction when it stood in the cold. The crystals melted at 160–161° after recrystallization from alcohol.

Found %: C 76.80, 76.53; H 4.87, 4.60. $C_{11}H_8O_2$. Calculated %: C 76.73; H 4.68.

In the literature [29] the melting point 160.5–161° is given for 1-naphthoic acid. A mixed melting point with a known sample gave no depression. The yield in different experiments was 0.5–1.5%.

Under analogous conditions, from 93.2 g (0.45 mole) 1-$C_{10}H_7Br$, 13.4 g (0.55 g-atom) magnesium, and 14.8 g (0.2 mole) ethyl formate was obtained 7 g (12.2%) naphthalene, 25 g (44%) 1,1-dinaphthylcarbinol with m.p. 140–141°, and 27 g (50.5%) 1,1-dinaphthylmethane.

B.p. 227–228° (3 mm), m.p. 106.5–107° (from alcohol or ether); according to the data of [2], m.p. 109°.
Found %: C 93.77, 94.00; H 5.99, 6.09. $C_{21}H_{16}$. Calculated %: C 93.99; H 6.01.
Melting point of 1,1-dinaphthylcarbinol after 1–2 recrystallizations from alcohol was raised to 147–147.5°; according to the data of [3], m.p. 146–147°.
Found %: C 88.74, 88.64; H 5.83, 5.79. $C_{21}H_{16}O$. Calculated %: C 88.70; H 5.67.

4. Reaction of ethyl acetate with n-decylmagnesium bromide. To the Grignard reagent, prepared in 75% yield from 26.8 g (1.1 g-atom) magnesium and 190 g (0.86 mole) of n-decyl bromide in 500 ml of ether, we added over 2 hours a solution of 29 g (0.33 mole) of ethyl acetate in 150 ml of ether. Stirring continued for 2 hours without heating; for 10 hours at the temperature of boiling ether. This was followed by the usual treatment of the reaction mixture and fractionation of the reaction products in a vacuum. We isolated 6.2 g (5%) of n-decane, 14 g (9.7%) of n-$C_{10}H_{21}OH$ (formed as a result of partial oxidation of the Grignard reagent by oxygen of the air), 4.2 g (1.8%) of n-eicosane, and also 64 g (61%) of methyl di-n-decylcarbinol.

B.p. 246–248° (7 mm), n_D^{20} 1.4543, d_4^{20} 0.8396.
Found %: C 81.20, 81.07; H 14.01, 14.08; OH 4.72. $C_{22}H_{46}O$. Calculated %: C 80.90; H 14.19; OH 4.91.

Heating 62 g of methyldidecylcarbinol with 8 g of anhydrous $CuSO_4$ for one hour at 175–180° gave 52 g of the corresponding olefin, with the composition $C_{22}H_{44}$.

B.p. 171° (1 mm), n_D^{20} 1.4526, d_4^{20} 0.7995.
Found %: C 85.63, 85.54; H 14.43, 14.39. $C_{22}H_{44}$. Calculated %: C 85.60; H 14.40.

The resulting olefin was hydrogenated over Raney nickel (initial hydrogen pressure 100 atm, 160–180°, 6 hours) and was converted into 11-methylheneicosane, which was twice distilled in a vacuum over sodium.

B.p. 186° (1 mm), m.p. 15–16°, n_D^{20} 1.4451, d_4^{20} 0.7942, MR_D 104.11; calc. 103.79.
Found %: C 85.29, 85.14; H 14.92, 14.90. $C_{22}H_{46}$. Calculated %: C 85.07; H 14.93.

SUMMARY

1. We have investigated the reaction of 1-naphthylmagnesium bromide with esters of n-monocarboxylic acids, and have shown that in distinction from n-decyl-, phenyl-, and biphenylmagnesium halides, 1-$C_{10}H_7MgBr$ reacts with the esters with formation, in addition to di-(1-naphthyl)alkylcarbinols (1',1'-di-(1-naphthyl)-1'-alkenes), of products of incomplete occurrence of the Grignard reaction, the corresponding alkyl 1-naphthyl ketones.

2. We have shown that the yields of alkyl 1-naphthyl ketones in these reactions increase, with simultaneous decrease in yields of dinaphthylalkenes, with decreasing dissociation constants of the acids whose esters were used in the reaction, and with increasing excess of 1-$C_{10}H_7MgBr$.

LITERATURE CITED

[1] L. Gattermann and F. Maffezzoli, Ber. 36, 4152 (1903).

[2] A Chichibabin, Ber. 44, 443 (1911).

[3] J. Schmidlin and P. Massini, Ber. 42, 2377 (1909).

[4] F. Blicke, J Am. Chem. Soc. 49, 2843 (1927).

[5] G. L. Stadnikov, Zhur. Russ. Khim. Obshch. 48, 1870 (1916); Ber. 57, 1 (1924).

[6] H. Ryan and J. Algar, Proc. Royal Irish Acad. 30, B, 97 (1913); Zbl. 1913, II, 2050.

[7] H. Ryan and T. Dillon, Proc. Royal Irish Acad. 29, B, 235 (1912); Zbl. 1913, II, 2049.

[8] W. Bachmann, J. Am. Chem. Soc. 54, 2112 (1932).

[9] E. Bergmann and W. Weiss, Ber. 64, 1485 (1931).

[10] N. Turkiewicz, Ber. 73, 861 (1940).

[11] I. I. Lapkin et al., Zhur. Obshchei Khim. 17, 1332, 1339 (1947); 18, 701 (1948).

[12] P. Pfeiffer and P. Schneider, J. pr. Ch. 129, 129 (1931).

[13] W. Parry, J. Chem. Soc. 99, 1169 (1911).

[14] S. R. Sergienko, L. N. Kvitkovskii, A. L. Tsedilina and Al. A. Petrov, Doklady Akad. Nauk SSSR 120, 541 (1958). •

[15] A. Schmidt and C. Hartmann, Ber. 74, 1325 (1941); V. V. Korshak, Zhur. Obshchei Khim. 9, 1470 (1939); H. Wienhaus and W. Treibs, Ber. 56, 1648 (1923); R. Lagrave, Ann. chim. (10), 8, 363 (1927); K. Ziegler et al., Lieb. Ann. 473, 1 (1929); 551, 150 (1942); W. Schlenk and E. Bergmann, Lieb. Ann. 479, 42 (1930); H. Masson, C. r. 135, 553 (1902); G. L. Stadnikov, Zhur. Russ. Khim. Obshch. 47, 2115 (1915).

[16] A. D. Petrov, E. P. Kaplan and Z. I. Letina, Zhur. Obshchei Khim. 26, 1246 (1956). •

[17] L.-B. T., II (1923, 1927, 1931).

[18] V. Grignard, C. r. 132, 336 (1901); Zbl. 1901, I, 612.

[19] A. E. Chichibabin, Zhur. Russ. Khim. Obshch. 37, 180 (1905); G. L. Stadnikov, Anomalous Grignard Reactions [in Russian] (Odessa, 1916).

[20] M. Kharasch and O. Reinmuth, Grignard Reactions of Nonmetallic Substances, (New York, 1954) p. 549.

[21] J. Herzenberg and E. von. Winterfeld, Ber. 64, 1036 (1931); V. Grignard, Ann. del'Université de Lyon, Neue Serie, 6, 1 (1901); Zbl. 1901, II, 622; A. Willemart, Ann. Chim. (10), 12, 345 (1929); Zbl. 1930, I, 1786; R. Larsen, R. Thorpe and F. Armfield, Ind. Eng. Ch. 34, 183 (1942); A. D. Petrov, O. M. Nefedov and V. D. Vorob'ev, Izv. Akad. Nauk SSSR, Otdel Khim. Nauk 1957, 1105; • F. Ullmann et al., Ber. 38, 2213 (1905).

[22] A. E. Chichibabin, Zhur. Russ. Khim. Obshch. 43, 1022 (1911).

[23] H. Zook et al., J. Am. Chem. Soc. 77, 4407 (1955).

[24] H. Gilman, Rec. trav. chim. 45, 314 (1926).

[25] O. M. Nefedov, Dissertation: D. I. Mendeleev Moscow State Technical Institute (Moscow, 1957).

[26] E. N. Novikova and L. N. Petrova, Zhur. Prikladnoi Khim. 23, 1336 (1947).

[27] L. Nunn and H. Henze, J. org. Chem. 12, 540 (1947).

[28] B. Bannister and B. Elsner, J. Chem. Soc. 1055 (1951).

[29] A. Kailan, Monatsh. 28, 1069 (1907).

• Original Russian pagination. See C B. Translation.

STUDIES IN LIPID CHEMISTRY

II. SYNTHESIS OF TRIGLYCERIDES OF VEGETABLE OILS

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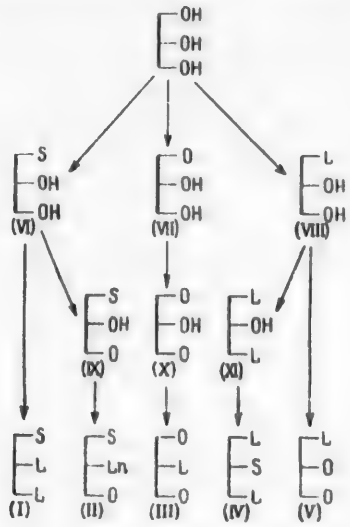
Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 3909–3911, 1959

Original article submitted November 27, 1958

In the present paper we describe the synthesis and the basic physico-chemical properties of α-stearo- β,α'-dilinolein (SLL) (I), α-stero-β-linoleno-α'-olein (SLnO) (II), α,α'-dioleo-β-linolein (OLO) (III), αα'-dilinoleo-β-stearin (LSL) (IV), and α-linoleo-βα'-diolein (LOO) (V), all of which contain four double bonds to the molecule, and all of which enter into the composition of a number of vegetable oils. The substances were prepared by esterification of the monoglycerides α-monostearin (VI), α-monoolein (VII), and α-monolinolein (VIII) with stearyl, oleyl, linoleyl, and linolenyl chlorides. As in the preceding communication *, the syntheses were, according to the required triglyceride structure effected in one stage (for SLL and LOO), or in two stages (for SLnO, OLO, and LSL), with intermediate preparation of the diglycerides. It can be concluded from these examples of glyceride synthesis that it is now possible to approach the investigation of natural mixtures of glycerides, i.e., of natural vegetable oils.



EXPERIMENTAL

1. α-Stearo-βα'-dilinolein (I). A solution of 13 g (0.0363 g-mole) of α-monostearin (VI) and 9.8 g of quinoline (0.076 g-mole) in 60 ml of chloroform was cooled in ice-water, and 22 g (0.0735 g-mole) of linoleyl

*Zhur. Obshchei Khim. 29, 11 (1959). [See C. B. translation].

chloride was added. The reaction mixture was boiled for 4 hr, cooled to 5–10°, and washed successively with 300 ml of 0.5 N sulfuric acid, 50 ml of water, and 50 ml of saturated aqueous sodium bicarbonate, and dried with sodium sulfate. The solvent was then distilled off under reduced pressure (15–20 mm). A yield of 29.1 g of crude triglyceride was obtained (I no. • 109.6). This product was purified by washing with ethanol at 60° (three 30 ml portions), and was then recrystallized from acetone (100 ml at -30° to -35°). Yield: 10.0 g (31.2%).

M.p.-(18–19)°, d_4^{20} 0.9186, n_D^{20} 1.4740, MR_D 270.2, calc. 268.52.
Found %: C 77.52; H 11.60. I. no. 114.3. $C_{57}H_{102}O_6F_4$. Calculated %: C 77.49; H 11.64. I no. 114.9.

2. α-Stearo-β-linoleo-α'olein (II). The reaction mixture contained 11 g (0.0176 g-mole) of α-stearo-α'-olein •• (IX), 7.5 g (0.0252 g-mole) of linoleyl chloride, and 4.4 g (0.0338 g-mole) of quinoline in 50 ml of chloroform. The yield of crude triglyceride obtained after washing the product with hot alcohol amounted to 11.0 g (I no. 110.3), and this was recrystallized from 110 ml of acetone at -20° to -18°, rejecting the first crop of crystals separating at -6° to -5°. Yield: 7.1 g (45.5%).

M.p.-8.5–9° and 14–14.5°, d_4^{20} 0.9208, n_D^{20} 1.4722, MR_D 268.7; calc. 268.52.
Found %: C 77.60; H 11.20. I no. 113.8. $C_{57}H_{102}O_6F_4$. Calculated %: C 77.49; H 11.64. I no. 114.9.

3. α,α'-dioleo-β-linolein (III). The starting material was αα'-diolein (X) •••, prepared from α-monoolein (VII) •••• and oleyl chloride •••••. The reaction mixture contained 17.2 g (0.0277 g-mole) of (X), 12.1 g (0.0405 g-mole) of linoleyl chloride, and 5.5 g (0.0423 g-mole) of quinoline in 50 ml of chloroform. The conditions of synthesis and purification of the triglyceride were as above. Yield: 17.6 g (71.9%).

M.p. 10–9°, d_4^{20} 0.9183, n_D^{20} 1.4720, MR_D 269.3; calc. 268.52.
Found %: C 77.55; H 11.77. I no. 114.4. $C_{57}H_{102}O_6F_4$. Calculated %: C 77.49; H 11.64. I no. 114.9.

4. α,α'-Dilinoleo-β-stearin (IV). A yield of 10.7 g of crude triglyceride was obtained from a reaction mixture of 7.3 g (0.0118 g-mole) of αα'-dilinolein (XI), 4 g (0.0132 g-mole) of stearyl chloride, and 2.2 g (0.0169 g-mole) of quinoline in 20 ml of chloroform. The product was washed with hot alcohol, and recrystallized from 70 ml of acetone at -35° to -30°. Yield: 6.2 g (59.3%).

M.p.-(3.5–2.5)°, d_4^{20} 0.9212, n_D^{20} 1.4742, MR_D 269.6; calc. 268.52.
Found %: C 77.49; H 11.79. I no. 114.8. $C_{57}H_{102}O_6F_4$. Calculated %: C 77.49; H 11.64. I no. 114.9.

5. α-Linoleo-βα'-diolein (V). This was, similarly to α-stearo-βα'-dilinolein (I), prepared by one-stage synthesis, without intermediate isolation of diglyceride. A yield of 34.4 g of crude triglyceride, I no. 109.6, was obtained from 14 g (0.0395 g-mole) of α-monolinolein (VIII), 24.2 g (0.0804 g-mole) of oleyl chloride, and 10.9 g (0.0845 g-mole) of quinoline in 56 ml of chloroform. The I no. rose to 111.9 after three washes with 30 ml portions of alcohol. The product was recrystallized from 150 ml of acetone at -55° to -50°, discarding the fraction separating at -20° to -15°. Yield: 21.9 g (62.8%).

M.p.-(2.5–2)°, d_4^{20} 0.9200, n_D^{20} 1.4740, MR_D 269.6; calc. 268.5.
Found %: C 77.18, 77.49; H 11.83, 11.71. I no. 114.2. $C_{57}H_{102}O_6F_4$. Calculated %: C 77.49; H 11.64; I no. 114.9.

SUMMARY

1. α-Stearo-βα'-dilinolein (SLL), α-stearo-β-linoleno-α'-olein (SLnO), αα'-dioleo-β-linolein (OLO), αα'-dilinoleo-β-stearin (LSL), and α-linoleo-βα'-diolein (LOO) have been synthesized.

2. The intermediate products α-monoolein, α-stearo-α'-olein, and αα'-diolein have been isolated and described.

•Iodine number

••M.p. 52–53°, I no. 40.55. $C_{39}H_{74}O_5F$ Calculated 40.74.

•••M.p. 21.5–22°, d_4^{22} 0.9244, n_D^{22} 1.4680, MR_D 186.73. $C_{39}H_{72}O_5F$ Calculated 186.2. I no. 81.3, Calc. 81.75.

••••M.p. 34–35°, I no. 70.8. $C_{21}H_{40}O_4F$. Calculated 71.2

•••••B.p. 154–155°/1 mm, d_4^{20} 0.9147, n_D^{20} 1.4646, MR_D 90.87. $C_{18}H_{33}OClF$. Calculated 90.10: I no. 83. 81, calcd. 84.36.

STUDIES IN LIPID CHEMISTRY

III. SYNTHESIS OF TRIGLYCERIDES OF VEGETABLE OILS

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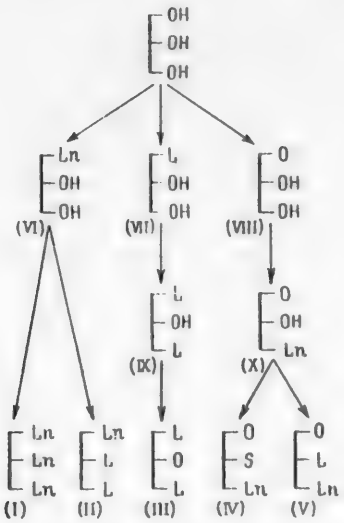
Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 3911–3913 December, 1959

Original article submitted December 29, 1958

In the present paper we describe the synthesis and the basic physicochemical properties of trilinolenin (LnLnLn) (I), α-linoleno-βα'-dilinolein (LnLL) (II), αα'-dilinoleo-β-olein (LOL) (III), α-oleo-β-stearo-α'-linolenin (OSLn) (IV), and α-oleo-β-linoleo-α'-linolenin (OLLn) (V); these products, as well as those described in our earlier communications, are components of natural vegetable oils [1–3].



The triglycerides (I) and (II) were prepared by direct esterification of α-monolinolenin (VI) with linolenyl or linoleyl chloride, in the presence of quinoline. The symmetrical triglyceride (III) was prepared from α-monolinolein (VII), with intermediate synthesis of αα'-dilinolein (IX). The mixed triglycerides (IV) and (V) were synthesized similarly, from α-monoolein (VIII) through α-oleo-α'-linolenin (X), which was reacted with stearyl or linoleyl chloride.

EXPERIMENTAL

1. Trilinolenin (I). We added 3.6 g (0.0121 g-mole) of linolenyl chloride • to a solution of 2 g (0.0057 g-mole) of α-monolinolenin (VI) •• and 1.6 g (0.0124 g-mole) of quinoline in 30 ml of chloroform at 2–3°. The

•d_4^{20} 0.9834, n_D^{20} 1.4845, MR_D 102.60. $C_{21}H_{36}O_4F_3$. Calculated 102.47; I no. 218; calc. 216.
••B.p. 136–137°(0.45 mm), d_4^{20} 0.9372, n_D^{20} 1.4812, MR_D 90.19. $C_{18}H_{29}OClF_3$. calc. 89.17

reaction mixture was heated to boiling for 4.5 hr in a stream of nitrogen, after which it was cooled to 10–15° and dissolved in 250 ml of ether, and the ethereal solution was washed successively with 15 ml of 5% sulfuric acid and 20 ml of 5% potassium carbonate solution. The solution was then dried with anhydrous sodium sulfate, and the solvent was distilled off, leaving 3.94 g of crude triglyceride (I no. 250.0). The product was then washed with 40 ml of methanol. Yield: 1.18 g (23.8%).

M.p. -(46–44)° and -(26–24)°, d_4^{20} 0.9591, n_D^{20} 1.4975, MR_D 266.7; calc. 266.19.

Found %: C 78.69, 78.19; H 10.30, 10.56. I no. 256.5. $C_{57}H_{92}O_5F_9$. Calculated %: C 78.39; H 10.62. I no. 261.6.

2. α-Linoleno-βα'-dilinolein (II). This was synthesized as for the preceding preparation, from 3.23 g (0.0092 g-mole) of (VI), 3.27 g (0.025 g-mole) of quinoline, and 6.55 g (0.022 g-mole) of linoleyl chloride in 30 ml of chloroform. The crude triglyceride (7.88 g, of I no. 181) was extracted with methanol (75 ml), to give 4.58 g of product of I no. 184, which was dissolved in 25 ml of ether, and the solution was passed through a chromatographic column packed with 50 g of alumina; adsorbed material was then eluted with 500 ml of ether. The eluate was filtered through 2 g of active charcoal, and the solvent was distilled off, leaving 2.28 g of product, of I no. 189.5. Further purification was effected by fractional crystallization from its solution in 14 ml of acetone. A fraction (0.16 g, of I no. 188.0) separated out at -40 to -35°. The mother liquor was then cooled down to -78°. A solid phase (0.45 g, of I no. 191.0) separated out, and was filtered off, and the solvent was distilled off from the filtrate. Yield 1.51 g (18.78%).

d_4^{20} 0.9494, n_D^{20} 1.4905, MR_D 267.4; calc. 267.12.

Found %: C 78.20, 78.06; H 10.74, 11.01. I no. 200.0. $C_{57}H_{96}O_6F_7$. Calculated %: C 78.03; H 11.02. I no. 202.6.

3. αα'-Dilinoleo-β-olein (III). This was prepared from 2.79 g (0.0045 g-mole) of αα'-dilinolein (IX) [1], 0.8 g (0.0062 g-mole) of quinoline, and 1.7 g (0.0056 g-mole) of oleyl chloride in 15 ml of chloroform. The reaction mixture was heated at the b.p. for 4.5 hr in a stream of nitrogen, and was then cooled down to 10–15° and dissolved in 200 ml of ether; the solution was washed successively with 10 ml of 5% sulfuric acid and 20 ml of aqueous potassium carbonate. The extract was dried over sodium sulfate, and the ether was distilled off, leaving 3.78 g of crude triglyceride (I no. 127). The product was washed with 30 ml of methanol, and fractionally crystallized from its solution in 8 ml of acetone. The mother liquor from a fraction depositing at -12 to -10° (0.73 g, of I no. 105.5) was cooled down to -65 to -60°, filtered, and the filtrate was freed of solvent. Yield of residue: 1.66 g (I no. 137.6). Recrystallization from 15 ml of acetone at -75 to -70° gave 1.06 g of product (26.6%).

M.p. -(40–38)°, d_4^{20} 0.9304, n_D^{20} 1.4781, MR_D 268.3; calc. 268.05

Found %: C 77.90, 77.93; H 11.11, 11.22. I no. 146. $C_{57}H_{100}O_6F_5$. Calculated %: C 77.64; H 11.44. I no. 144.

4. α-Oleo-β-stearo-α'-linolenin (IV). α-Oleo-α'-linolenin (X)* was prepared from α-monoolein (VIII) and linolenyl chloride. Under conditions similar to those specified for preparation (III), a reaction mixture of 25 g (0.0405 g-mole) of (X), 6 g (0.0464 g-mole) of quinoline, and 14 g (0.0462 g-mole) of stearyl chloride in 100 ml of chloroform gave 33.8 g of crude triglyceride (I no. 102.3), which was washed with three 30-ml portions of methanol, and recrystallized from 150 ml of acetone at -30 to -25°, discarding the fraction separating out at -15 to -10°. The product was further purified by passing its solution in 10 volumes of ether through a column packed with alumina and active charcoal. Yield 7.4 g (20.7%).

M.p. 4.5–6°, d_4^{20} 0.9140, n_D^{20} 1.4708, MR_D 269.9; calc. 268.5.

Found %: C 77.31, 77.30; H 11.54, 11.64. I no. 113.9. $C_{57}H_{102}O_6F_4$. Calculated %: C 77.50; H 11.63. I no. 114.9.

5. α-Oleo-β-linoleo-α'-linolenin (V). A mixture of 23 g (0.0373 g-mole) of (X), 12.5 g (0.0418 g-mole) of linoleyl chloride and 5.5 g (0.0426 g-mole) of quinoline in 100 ml of chloroform gave 31.8 g of triglyceride (I no. 259.9). The product was extracted with alcohol and then recrystallized from acetone at -65 to -60°, discarding the fraction separating out at -35 to -30°; the product was further purified by passing its ethereal solution through a column packed with alumina and active charcoal. Yield of pure triglyceride 5.6 g (17.1%).

*M.p. -(11–10)°, d_4^{20} 0.9349, n_D^{20} 1.4772, MR_D 186.5. $C_{39}H_{68}O_5F_4$. Calc. 185.3

M.p.-(30.5—29)°, d_4^{20} 0.9269, n_D^{20} 1.4792, MR_D 269.1; calc. 267.6.

Found %: C 77.92, 77.63; H 11.31, 11.37. I no. 172.7. $C_{57}H_{98}O_6$ F_8. Calculated %: C 77.85; H 11.23. I no. 173.2.

SUMMARY

The following have been synthesized: Trilinolenin (LnLnLn), α-linoleno-βα'-dilinolein (LnLL), αα'-dilinoleo-β-olein (LOL), α-oleo-β-stearo-α'-linolenin (OSLn), and α-oleo-β-linoleo-α'-linolenin (OLLn).

LITERATURE CITED

[1] I. K. Sarycheva, O. V. Utkina, M. E. Maurit, G. A. Vorob'eva, M. N. Vargaftik, A. I. Sherle, N. A. Krit and N. A. Preobrazhenskii, Zhur. Obshchei Khim. 29, 3583 (1959). *

[2] M. E. Maurit, I. K. Sarycheva and N. A. Preobrazhenskii, Zhur. Obshchei Khim. 29, 3909 (1959). *

[3] H. I. Dutton and I. A. Cannon, J. Am. Oil Chem. Soc. 33, 46 (1956); C. R. Scholfield and H. I. Dutton, J. Am. Oil. Chem. Soc. 35, 493 (1958).

* Original Russian pagination. See C. B. Translation

STEREOCHEMISTRY OF NITROGEN-CONTAINING HETEROCYCLES

VI. STEREOISOMERISM OF 2,3,6-TRIMETHYL-4-PIPERIDONE AND OF THE ANALOGOUS 2,3,6-TRIMETHYL-4-PIPERIDOL

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Translated from Zhur. Obshchei Khim. Vol. 29, No. 12, pp. 3913-3921, December, 1959

Original article submitted October 6, 1958.

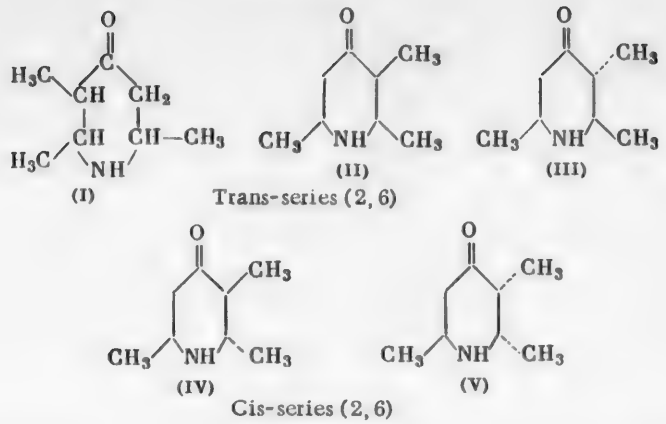
In an earlier publication we described the stereoisomerism of 2,5-dimethyl-4-piperidone and of the corresponding 2,5-dimethyl-4-piperidol; local anesthetics of the tropine type were prepared from the stereoisomeric alcohols [1]. Pharmacological tests showed that these products were all of high physiological activity, of the order of that of cocaine, and that, as was expected, these properties were to a considerable extent dependent on the spatial structure of their molecules. It was also found that, with certain exceptions, these synthetic products were of high toxicity, and had a strongly irritating action, for which reasons they were unacceptable for medicinal use [2]. It is possible that the high toxicity and the other undesirable properties of these products may be to some extent related to the presence of alkyl substituents at the carbon atoms of the piperidine ring; such substituents are absent from cocaine and its companion alkaloids (tropacocaine, atropine, and others).

It was, inview of this possibility, of interest to examine the effect on the anesthetic and toxic properties of anesthetics of the piperidine series of increasing the number of substituents, and in particular of introducing three methyl groups at different carbon atoms of the piperidine ring. In connection with this investigation, we first made a study of the stereoisomerism of 2,3,6-trimethyl-4-piperidone and of 2,3,6-trimethyl-4-piperidol, which were used as the starting materials for the synthesis of the above-mentioned local anesthetics. Such stereochemical studies were also of intrinsic interest, in particular for the theory of conformational analysis [3] and for its application to piperidine derivatives.

2,3,6-Trimethyl-4-piperidone (I) was prepared by the method of reference [4], introducing some modifications into the last stage of the synthesis which raised the yield to 65%. The substance (I) contains three asymmetric carbon atoms, four racemic forms of which should theoretically be possible (Scheme 1). We were able to separate the hydrochloride of (I) into three salts, of m.p. 191° (74.5%), 154° (6.1%), and 156° (0.12%). The mixed m.p. of the last two hydrochlorides was much lower than that of either of them, suggesting that these salts are derived from different racemates. When the hydrochloride melting at 154° was heated to 165° the molten mass resolidified, undergoing quantitative conversion into the hydrochloride of m.p. 191°. When boiled with concentrated hydrochloric acid, 12% of the latter was converted into the isomer melting at 154°.

The relatively ready interconvertibility of two of the racemates of the piperidone derivative (I), through the hydrochlorides, suggests that these two isomers should have an identical, stable configuration of methyl radicals at carbon atoms 2 and 6, but should differ in the spatial arrangement of the third methyl group. These conditions are satisfied by the structures of the first two racemates, (II) and (III), which belong to the trans-series of ketones of Scheme 1. In accordance with the principles of conformational analysis, their 2,6-methyl radicals should be disposed equatorially, and the third methyl radical should be oriented equatorially or axially in (II) and (III), respectively.

SCHEME 1

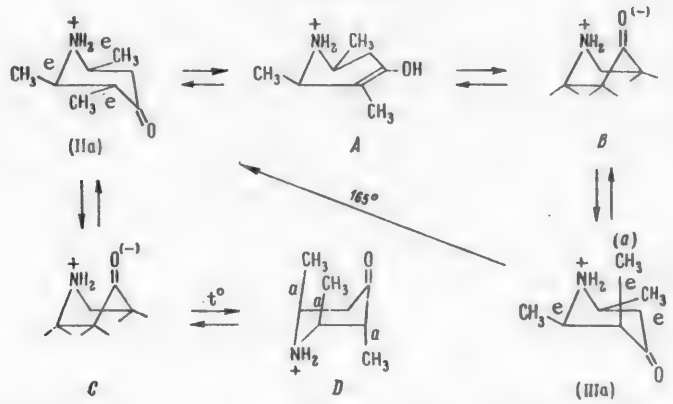


Trans-series (2, 6)

Cis-series (2, 6)

The mutual interconversions of the hydrochlorides of the stereoisomeric ketones (II) and (III) appear to involve the same principles and the same transformations as were earlier established in our laboratory for the isomerism of the hydrochlorides of the racemates of 2-methyl-4-ketodecahydroquinoline [5], viz., an essential condition for the isomerization of the stable conformation (IIa) to the less stable (IIIa) is the presence of an aqueous medium, in which an equilibrium is established between (IIa) and (IIIa), with intermediate formation of configurations A and B. Reconversion of the hydrochloride of (IIIa) into that of (IIa) is evidently achieved via the enolic form A, at high temperature. The isomeric transformations of the hydrochlorides, (IIa) ⇌(IIIa), are thus reducible to the reversible displacement of the equatorial methyl group of (IIa) to an axial configuration in (IIIa) (Scheme 2).

SCHEME 2*



Other transformations, not involving intermediate formation of an enolic form, are quite possible, such as toward formation of C and D, when the stable racemate (IIa) is heated with hydrochloric acid. Such transformations may, in fact, be of greater importance than those involving the intermediates A and B, since hydrochloric acid undoubtedly suppresses enolization, which may be an explanation of the low yield (12%) of racemate (IIIa). The process involving the C ⇌D transformations is not, however, properly speaking one of isomerization, since it represents only the usual thermal conversion of a six-membered cycle, with formation of excited molecules.

It is of interest that the racemates (II) and (III) are stable when present as the bases, and do not change their conformations when subjected to fractionation; this distinguishes them from the isomers of 2,5-dimethyl-4-piperidone [1].

When heated at temperatures higher than its m.p., the third hydrochloride (m.p. 156°) did not undergo isomerization; this substance appears to be a derivative of either racemate (IV) or racemate (V), belonging to the cis-series. We were not able to prepare a pure specimen of this base, because of the insufficient amount of salt available to us.

* Here e = equatorial; a = axial.

TABLE 1

Racemates (II) and (III)	Physiochemical properties of the ketones					Melting point		
	boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	picrate	hydrochloride	oxime hydrochloride
Ketone (IIa)	65.5° (1)	1.4625	0.95248	40.79	40.56	163°	191°	230°
Ketone (IIIa)	62 (1)	1.4680	0.96568	40.62		171	154	215

The above-described results show that when trisubstituted monocyclic γ-piperidones are synthesized by Nazarov's method [3] the products consist chiefly (over 80%) of racemates of the trans-configuration, with only very small yields of the theoretically envisaged cis-series racemates, with an e,a configuration of the substituents at carbon atoms 2 and 6 of the piperidine ring. The axial (cis-) position of the methyl group at the third carbon atom of isomer (IIIa) is confirmed by the higher refractive index and density of this isomer, as compared with (IIa), this being characteristic of cis-isomers, in accordance with Auwers' rule [6] (Table 1).

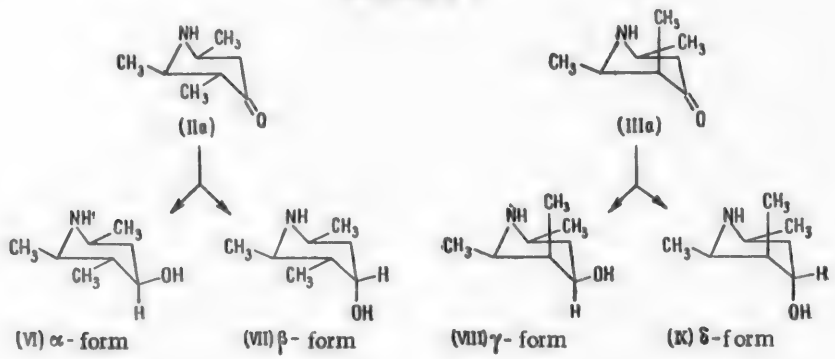
We were able, using various methods for the reduction of the stereoisomeric ketones (IIa) and (IIIa), to prepare all four theoretically possible racemates of 2,3,6-trimethyl-4-piperidol, designated as the α-, β-, γ-, and δ-forms, and corresponding in structure to the two ketones from which they were prepared. The melting points of these piperidols and of some of their crystalline derivatives are given in Table 2.

TABLE 2

Derivative	Melting point of bases			
	135—136° (VI) (α)	146—147° (VII) (β)	89—90° (VIII) (γ)	109—110° (IX) (δ)
	Melting point of derivatives			
Hydrochloride	290—291°	229—230°	206—207°	217—218°
Picrate	176—177	174—175	166—167	169—170

The α- (VI) and β-forms (VII) were obtained, in 68.3 and 7.7% yield, respectively, by hydrogenation of the ketone (IIa) in the presence of a nickel catalyst. Reduction of the same ketone with sodium in absolute alcohol gave chiefly the α-piperidol (VI), m.p. 136° (63.8%), with not more than 5% yields of the β-piperidol (VII), m.p. 147°. Reduction of ketone (IIa) with aluminum isopropoxide gave a mixture of isomers, from which we isolated β-piperidol (VII) in 47.7% yield, but were unable to separate any α-piperidol (VI). The difficultly separable mixture of α- and β-piperidols obtained by reduction of the ketone (IIa) was isomerized by treatment with sodium isopentoxide, to give about a 60% yield of pure α-form (VI).

SCHEME 3



It may be supposed that only the β-form underwent isomerization in this reaction, thus leading to increase in the yield of α-form. It may hence be concluded that, in accordance with the Auwers–Skitta rule, α-piperidol (VI) is the stable form, and should, in accordance with Hassel's rule, have the hydroxyl disposed equatorially.

Reduction of the second isomeric piperidone (IIIa) in the presence of nickel catalyst gave a mixture of γ- and δ-piperidols, in the form of an uncrystallizable oil, from which we were able, through its hydrochloride, to separate the δ-form (IX), m.p. 110°. The second piperidol (VIII), m.p. 90°, was obtained in 55% yield by reduction of ketone (IIIa) with sodium in absolute alcohol.

Scheme 3 gives the conformations of the four piperidols (VI–IX), as based on their properties and on the conditions of their preparation from the ketones (IIa) and (IIIa).

EXPERIMENTAL

2,3,6-Trimethyl-4-piperidone (I). Condensation of vinylacetylene with methyl ethyl ketone, dehydration of 5-methylhept-1-en-3-yn-5-ol, and hydration of 5-methylhepta-1,5-dien-3-yne, were accomplished as described in [7]. Cyclization of the resulting dienone and its methoxy derivative with ammonia was achieved in the following way. A mixture (45.5 g) of 5-methylhepta-1,5-dien-4-one and 2-methoxy-5-methylhept-5-en-4-one (b.p. 74–85°/7 mm; n_D^{20} 1.4600) in 800 ml of 25% ammonia was heated on a boiling-water bath for 8 hours, in a liter autoclave. Excess ammonia and most of the water were removed by distillation in a low vacuum. The residue was made neutral with 1:1 hydrochloric acid, the solution was washed repeatedly with ether, and the base was liberated by adding an excess of strong caustic soda. The base was taken up in ether, the extract was dried with ignited potassium carbonate, the solvent was distilled off, and the residue was vacuum distilled. We obtained a yield of 61.9% of substance (I), b.p. 74–77°/3 mm, n_D^{20} 1.4700. Yields of 65% or more were obtained in many of the batches. Altogether, we thus synthesized about 1 kg of piperidone (I). *

Separation of the mixture of isomeric 2,3,6-trimethylpiperidones (I) as their hydrochlorides [preparation of hydrochlorides of II (m.p. 191°, III (m.p. 154°), and IV (m.p. 156°)]. A solution of 843 g of crude 2,3,6-trimethyl-4-piperidone (I) in 2100 ml of acetone was neutralized with concentrated hydrochloric acid, with cooling. The crystals of hydrochloride separating were collected and washed with acetone. We obtained 422 g of hydrochloride of (II), m.p. 190–191°, in the form of a fine powder.

Found %: N 7.42, 7.28. $C_8H_{16}ONCl$. Calculated %: N 7.88.

The mother liquor was evaporated to dryness, the residual hydrochlorides were dissolved in water, and the solution was repeatedly extracted with ether. We thus extracted 56 g of neutral products. The aqueous solution of hydrochlorides was treated with saturated aqueous potassium carbonate, liberating the base (I), which was isolated as described above (450.5 g, b.p. 74–80°/3 mm; n_D^{20} 1.4655), dissolved in 1500 ml of acetone, and treated with dry hydrogen chloride. A further 283.5 g of hydrochloride of (II), m.p. 190–191°, was collected after standing for 24 hr. The mother liquor was evaporated down to one-third of its initial volume, and allowed to crystallize; 70 g of hydrochloride of (III), m.p. 153–154°, separated in the form of small, lustrous floccules.

Found %: N 7.39, 7.42. $C_8H_{16}ONCl$. Calculated %: N 7.88.

A hydrochloride fraction of m.p. 127–132° separated out after further concentration of the mother liquors. All the batches of this product were pooled and heated at 160–170° for 30 minutes. A solution of the cooled melt in acetone gave a further 29.5 g of hydrochloride of (II), m.p. 190–191°. Repeated fractional crystallizations of the residual hydrochlorides from acetone gave 1.1 g of the hydrochloride of piperidone (IV), short needles, m.p. 155–156°, mixed m.p. with hydrochlorides of (II) and (III) respectively 130–135° and 127–132°.

Found %: N 7.81, 8.08. $C_8H_{16}ONCl$. Calculated %: N 7.88.

We thus obtained a total yield of 735 g (74.5%) of hydrochloride of (II), 70 g (6.1%) of hydrochloride of (III), and 1.1 g (0.12%) of trimethylpiperidone hydrochloride of (IV). There remained 152 g (15.4%) of hydrochlorides unseparated.

*M. N. Akomova helped in the preparation of the piperidone. All the analyses were performed in the Microchemical Laboratory of the Institute, under the direction of M. K. Dzhamaletdinova.

Preparation of isomer (IIa) of 2,3,6-trimethyl-4-piperidone. We dissolved 70 g of (IIa) hydrochloride, m.p. 190–191°, in 100 ml of water, and added aqueous potassium carbonate to liberate the base. The base was extracted with ether, the solution was dried over ignited potassium carbonate, the solvent was distilled off, and the residue was vacuum distilled. Yield of (IIa): 53.7 g.

B.p. 65.5–66° (1 mm), n_D^{20} 1.4625, d_4^{20} 0.9524, MR_D 40.79; calc. 40.56.
Found %: C 67.42, 67.60; H 10.87, 11.01; N 9.76, 9.62. $C_8H_{15}ON$. Calculated %: C 68.04; H 10.71; N 9.92.

The hydrochloride was obtained in 94.3% yield by saturating an acetone solution of (IIa) with dry hydrogen chloride; the product was a finely crystalline powder, melting at 190–191°, and not giving any depression of m.p. when mixed with an authentic specimen of (IIa) hydrochloride; sparingly soluble in acetone and alcohol.

The picrate was obtained in 96.9% yield by dissolving 0.4 g of picric acid in a solution of 0.25 g of product (IIa) in 3 ml of methanol. Small yellow crystals, m.p. 162–163°.

Found %: N 14.95, 15.35. $C_{14}H_{18}O_8N_4$. Calculated %: N 15.13.

The oxime hydrochloride was prepared by dissolving 0.7 g of product (IIa) in a hot solution of 0.35 g of hydroxylamine hydrochloride in 15 ml of absolute alcohol. Small crystals, m.p. 229–230° (from absolute alcohol).

Found %: N 14.25, 14.30. $C_8H_{17}ON_2Cl$. Calculated %: N 14.45.

Preparation of isomer (IIIa) of 2,3,6-trimethyl-4-piperidone. Potassium carbonate was added to a solution of 37.2 g of (IIIa) hydrochloride (m.p. 153–154°), and the liberated base was treated as above. Yield: 28.7 g of (IIIa).

B.p. 62–62.5° (1 mm), n_D^{20} 1.4680, d_4^{20} 0.96568, MR_D 40.62; calc. 40.56.
Found %: N 9.67, 9.78. $C_8H_{15}ON$. Calculated %: N 9.92.

Hydrochloride: small, lustrous floccules, m.p. 153–154° (from acetone), giving no m.p. depression with an authentic specimen. It differs from (IIa) hydrochloride in being readily soluble in alcohol and dichloroethane; it is soluble in hot acetone.

Picrate: large yellow crystals, m.p. 170–171° (from methanol).

Found %: N 15.42, 15.59. $C_{14}H_{18}O_8N_4$. Calculated %: N 15.13.

The oxime hydrochloride was prepared as described above: microcrystalline powder, m.p. 214–215° (from absolute alcohol).

Found %: N 14.11, 14.31. $C_8H_{17}ON_2Cl$. Calculated %: N 14.45.

Isomerization of 2,3,6-trimethyl-4-piperidone (III) hydrochloride, of m.p. 154°, into 2,3,6-trimethyl-4-piperidone (II) hydrochloride, of m.p. 191°. We placed 0.1 g of (III) hydrochloride, m.p. 153–154°, into a small tube, which was evacuated by means of an oil vacuum pump, sealed, and heated at 156–165° for 30 minutes. The initially molten hydrochloride resolidified at 165°. The product was washed with acetone. We obtained 0.09 g of (II) hydrochloride, m.p. 190–191°, giving no depression of m.p. when mixed with an authentic specimen.

Isomerization of 2,3,6-trimethyl-4-piperidone (II) hydrochloride, m.p. 190–191°, into 2,3,6-trimethyl-4-piperidone (III) hydrochloride, m.p. 154°, when heated with hydrochloric acid. We dissolved 102.4 g of hydrochloride of m.p. 190–191° in 100 ml of concentrated hydrochloric acid, and heated on a boiling-water bath for 72 hours. The solution was then evaporated to dryness under reduced pressure (water pump), and the residue was extracted with hot acetone (1500 ml), and on cooling deposited 70.7 g of unchanged (II) hydrochloride, m.p. 190–191°. By progressive concentration of the mother liquors we obtained a total of 12.84 g (12.5%) of (III) hydrochloride, m.p. 153–154°.

Hydrogenation of 2,3,6-trimethyl-4-piperidone (IIa) in the presence of nickel catalyst. A solution of 20 g of piperidone (IIa) in 100 ml of alcohol was hydrogenated in the presence of Raney nickel catalyst, prepared from 10 g of nickel–aluminum alloy. After 3.5 hours of shaking, 3.6 liters of hydrogen had been absorbed, as compared with the theoretical amount of 3.62 liters. The catalyst was filtered off, the filtrate was evaporated to dryness under reduced pressure, and the residue was fractionally recrystallized from acetone. We obtained 13.15 g (68.3%) of the α-form (VI), as large prisms, m.p. 135–136°.

Found %: C 67.43, 67.29; H 11.91, 11.93; N 9.39, 9.51. $C_8H_{17}ON$. Calculated %: C 67.08; H 11.96; N 9.78.

Hydrochloride: finely crystalline powder, m.p. 290–291° (from absolute alcohol).

Found %: N 7.10, 7.31. $C_8H_{18}ONCl$. Calculated %: N 7.80.

Picrate: by adding a hot solution of piperidol (VI) in methanol to the calculated amount of picric acid; yellow prisms, m.p. 176–177° (from methanol).

Found %: N 14.94, 14.86. $C_{14}H_{20}O_8N_4$. Calculated %: N 15.05.

From the mother liquor remaining after the α-form had separated out, we obtained 1.49 g (7.73%) of β-form (VII); thin, transparent platelets, m.p. 146–147° (from acetone).

Found %: N 9.40, 9.26. $C_8H_{17}ON$. Calculated %: N 9.78.

The hydrochloride was prepared by saturating a solution of piperidol (VII) in alcohol with hydrogen chloride, and adding ether to precipitate out the product; crystals, m.p. 229–230°.

Found %: N 7.52, 7.53. $C_8H_{18}ONCl$. Calculated %: N 7.80.

Picrate: yellow crystals, m.p. 174–175° (precipitated from methanol by ether); mixed m.p. with α-piperidol (VI) picrate (m.p. 176–177°), 143–146°.

Found %: N 14.86, 14.71. $C_{14}H_{20}O_8N_4$. Calculated %: N 15.05.

Reduction of 2,3,6-trimethyl-4-piperidone (IIa) with sodium in alcoholic solution. We added 60 g of sodium, in small portions, to a solution of 20 g of racemic piperidone (IIa) in 700 ml of absolute alcohol, in a flask fitted with a reflux condenser. After all the sodium had been added, the mixture acquired a pasty consistency, and was heated until all the sodium had reacted. After cooling, the reaction mixture was made acid with hydrochloric acid. The sodium chloride precipitating out was collected on the filter, and washed with a few portions of hot alcohol; the aqueous alcoholic filtrate was evaporated to dryness under slightly reduced pressure. The dry residue was dissolved in 100 ml of water, the solution was extracted with two portions of ether, and the aqueous layer was made alkaline with potassium carbonate. The free base was taken up in ether, the extract was dried over ignited potassium carbonate, filtered, and concentrated down to three-quarters of its initial volume. The crystals separating out after standing were recrystallized from acetone. We obtained 12.3 g (63.8%) of α-form (VI), m.p. 135–136°, not giving any depression of m.p. when mixed with an authentic specimen. The ethereal mother liquor was evaporated down to dryness, and the residue was recrystallized from acetone, giving 0.89 g (4.6%) of the β-form of piperidol (VII), m.p. 146–147°.

Reduction of 2,3,6-trimethyl-4-piperidone (IIa) with aluminum isopropoxide. We placed 28.2 g of piperidone (IIa) and 100 ml of 1 M aluminum isopropoxide in dry isopropyl alcohol into a 250 ml round-bottomed flask, fitted with a reflux condenser through which hot water (60°) was being passed, connected at the upper end with a second, inclined condenser through which cold water was passed [8]. The mixture was heated on a Wood's alloy bath for 15 hours, until the distillate no longer gave a positive test for acetone (with 2,4-dinitrophenylhydrazine). Excess of isopropyl alcohol was distilled off under reduced pressure, and the foamy residue was taken up in 100 ml of water, and treated with solid sodium hydroxide. The semisolid base which rose to the surface was taken up in ether, crystallized out, and purified by repeated recrystallization from acetone. We obtained 13.65 g (47.7%) of crystalline β-form of piperidol (VIII), melting at 146–147°, and not depressing the m.p. of an authentic specimen of β-form.

Isomerization of a mixture of α- and β-forms of 2,3,6-trimethyl-4-piperidol, (VI) and (VII). We added 14.2 g of the difficultly separable mixture of α- and β-forms of piperidol, (VI) and (VII), melting at 115–120°, left over from the above-described processes of reduction of piperidone (IIa), to a solution prepared by dissolving 21 g of sodium in 300 ml of isoamyl alcohol, and heated the mixture at 190–220° for 53 hours. The cooled product was shaken with 50 ml of water, and the alcohol layer separating out was evaporated down to a third of its original volume, and extracted with 10% hydrochloric acid until it gave a neutral reaction. The combined aqueous extracts were evaporated down to a small volume, and treated with potassium carbonate. The free bases were taken up in ether, the ethereal solution was dried with ignited potassium carbonate, the solvent was distilled off, and the residue was twice recrystallized from acetone. We thus obtained 4.4 g of crystalline α-form of piperidol (VI), m.p. 135–136°. The remaining isoamyl alcohol solution was shaken with a further 100 ml of 10% hydrochloric acid, and the

aqueous extract was treated with potassium carbonate, as before. The base so obtained had a dark color, however, and did not crystallize satisfactorily from acetone; it was therefore converted into the hydrochloride by saturating its alcoholic solution with hydrogen chloride, precipitating out the product with ether. We obtained 4.54 g of the hydrochloride of the α-form of piperidol (VI), m.p. 289–290°, which did not depress the m.p. of a specimen of hydrochloride prepared as above.

Reduction of 2,3,6-trimethyl-4-piperidone (IIIa) with sodium in alcoholic solution. We added 70 g of sodium to a solution of racemic piperidone (IIIa) in 700 ml of absolute alcohol, and treated the reaction product as described above. We obtained 27.8 g (96.5%) of a mixture of isomers, from which 15.3 g (54.7%) of the γ-form of piperidol (VIII), m.p. 89–90°, was obtained by fractional crystallization from petroleum ether (b.p. 60–70°).

Found %: C 68.54, 68.30; H 12.1, 12.29; N 9.92, 9.78. $C_8H_{17}ON$. Calculated %: C 67.08; H 11.96; N 9.78.

The hydrochloride was prepared in 97.6% yield by saturating a solution of 0.5 g of piperidol (VIII) in alcohol with dry hydrogen chloride, and precipitating out the product with ether. Finely crystalline powder, m.p. 206–207°.

Found %: N 7.94, 7.84. $C_8H_{18}ONCl$. Calculated %: N 7.80.

Picrate: yellow crystals, m.p. 166–167° (precipitated from alcohol by ether).

Found %: N 14.96, 15.28. $C_{14}H_{20}O_8N_4$. Calculated %: N 15.05.

Hydrogenation of 2,3,6-trimethyl-4-piperidone (IIIa) in the presence of nickel catalyst. A solution of 22.9 g of piperidone (IIIa) in 100 ml of alcohol was hydrogenated, using Raney nickel catalyst prepared from 10 g of alloy. The amount of hydrogen absorbed at the end of 25 hours was 3.55 liters, as compared with the theoretical requirement of 3.63 liters. The catalyst was filtered off, the solvent was removed from the filtrate, and the residual uncrystallizable oil was vacuum distilled. The heavy, colorless oil distilling over was converted into the hydrochloride, which after repeated recrystallization from alcohol gave 3.43 g of 2,3,6-trimethyl-4-piperidol (IX) hydrochloride, m.p. 217–218°, mixed m.p. with piperidol (VIII) hyrochloride (m.p. 206–207°),202–204°.

Found %: N 7.57, 7.44. $C_8H_{18}ONCl$. Calculated %: N 7.80.

Treatment of this hydrochloride with potassium carbonate gave crystalline δ-form of piperidol (IX), platelets melting at 109–110° (from petroleum ether boiling at 60–70°).

Found %: N 9.87, 9.92. $C_8H_{17}ON$. Calculated %: N 9.78.

Picrate: large yellow crystals, m.p. 169–170° (crystallized from methanol after addition of ether).

Found %: N 14.48, 14.54. $C_{14}H_{20}O_8N_4$. Calculated %: N 15.05.

SUMMARY

1. Two of the four theoretically possible stereoisomers of 2,3,6-trimethyl-4-piperidone have been prepared, and the conditions required for their mutual interconversions through the hydrochlorides have been examined.

2. All of the four possible stereoisomers of 2,3,6-trimethyl-4-piperidol have been prepared by the reduction of the two stereoisomeric piperidones, and their structure has been described in terms of the principles of conformational analysis.

LITERATURE CITED

[1] I. N. Nazarov, D. V. Sokolov and V. N. Rakcheeva, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk, 80 (1954). •

[2] M. N. Gordin and G. I. Samarina, Izvest. Akad. Nauk Kazakh. SSR, No. 4, 97 (1954).

[3] I. N. Nazarov and L. D. Bergel'son, Usp. Khimii 26, 3 (1957); D. R. Barton and R. C. Cookson, Quart. Rev. 10, 44 (1956).

• Original Russian pagination. See C. B. Translation.

[4] I. N. Nazarov and V. A. Rudenko, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk, 610 (1948).

[5] D. V. Sokolov, G. S. Litvinenko and K. I. Khludneva, Zhur. Obshchei Khim. 29, 1112 (1959). •

[6] Von Auwers, Dersch, J. prakt. Chem. 124, 209 (1930).

[7] I. N. Nazarov and I. I. Zaretskaya, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk No. 5, 529 (1946).

[8] Organic Reactions [in Russian], Vol. 2, 194 (1950).

• Original Russian pagination. See C. B. Translation

INVESTIGATION IN THE FIELD OF SUBSTITUTED VINYL ETHERS.

COMMUNICATION II. SYNTHESIS OF α-SUBSTITUTED VINYL BUTYL ETHERS.

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Translated from Zhurnal Obschei Khimii, Vol. 29, No. 12, pp. 3922-3926, December, 1959

Original article submitted November 20, 1958

The simple vinyl alkyl ethers are well known for their extremely high reactivity and have been investigated adequately [1]. As regards the α-substituted vinyl alkyl ethers, they are not readily available and are practically undescribed in the literature. Their capability of both polymerization and copolymerization is of especial interest. We have previously described [2] the synthesis of α-substituted vinyl ethyl ethers. In the present work we have carried out the preparation of α-substituted vinyl butyl ethers.

There are directions for the synthesis of three representatives of this class of compounds in the literature. α-Methylvinyl butyl ether was prepared [3] by splitting out hydrogen bromide from α-methyl-β-bromoethyl butyl ether. This same ether was obtained [4] by condensation of butyl alcohol with methylacetylene. α-Butyl- and α-isobutylvinyl butyl ethers were prepared [5] by heating the corresponding ketals in the presence of p-toluenesulfonic acid.

We carried out the synthesis of α-substituted vinyl butyl ethers by the following scheme:

$$CH_2{=}CH{-}OC_4H_9 \xrightarrow{Br_2} CH_2Br{-}CHBr{-}OC_4H_9 \xrightarrow{R'MgX}$$
$$\longrightarrow CH_2Br{-}\underset{\displaystyle R'}{\underset{|}{CH}}{-}OC_4H_9 \xrightarrow{-HBr} CH_2{=}\underset{\displaystyle R'}{\underset{|}{C}}{-}OC_4H_9.$$

The splitting out of hydrogen bromide goes well when the β-bromoalkyl ethers are heated for 2-2.5 hours at a temperature close to their boiling point. To avoid hydrolysis of the substituted vinyl ethers under the influence of potassium bromide, it is necessary to use a large excess of pulverized potassium hydroxide. It must be noted that β-bromoalkyl ethers with a large alkyl radical split out hydrogen bromide more easily than those with small radicals. Apparently, this is connected with the fact that as the alkyl radical becomes larger, the C–Br bond becomes weaker.

The α-substituted vinyl butyl ethers were colorless mobile liquids with a pleasant odor. Like the simple vinyl alkyl ethers, they were easily hydrolyzed with the formation of the corresponding ketones. The Raman spectra of the α-butyl- and α-isobutylvinyl butyl ethers obtained were studied (Table 1). If we compare the spectra of the substituted vinyl ethers with those of the simple vinyl butyl ether, it can be readily noted that for the vinyl butyl ether the region of the C = C bond is represented by a triplet, and for the α-substituted ethers it is represented by a doublet, while the line corresponding to the highest frequency (1653) remains unchanged in the two groups of compounds.

EXPERIMENTAL

α,β-Dibromoethyl butyl ether was prepared by brominating vinyl butyl ether [6].

α-Ethyl-β-bromoethyl butyl ether. To the organomagnesium compound obtained from 15 g of Mg and 70 g of C_2H_5Br was added dropwise, at 0°, 160 g of α,β-dibromoethyl butyl ether diluted with an equal volume of dry

ether. The mixture was left for 10-12 hours at room temperature. Hydrolysis was carried out with ice. The aqueous layer was treated with 10% hydrochloric acid solution, and then extracted with ether. The ether layer was washed with 20% sodium hydroxide solution and water. It was dried over calcium chloride. After the ethyl ether was distilled off, the residue was distilled in vacuo. The following fractions were obtained:

First, b. p. 40-80° (13 mm), 5.61 g, n_4^{20} 1.4020; 2nd, b. p. 80-81° (13 mm), 185.6 g, n_D^{20} 1.4460.

After repeated distillation of the 2nd fraction over sodium, α-ethyl-β-bromoethyl butyl ether was obtained with the constants shown in Table 2; the constants and yields of other representatives of the β-bromoalkyl ethers obtained in a similar manner are given in the same table.

α-Propylvinyl butyl ether. One hundred grams of α-propyl-β-bromoethyl butyl ether and 100 g of pulverized potassium hydroxide were placed in a copper flask. The mixture was heated for 2 hours at 190-200°. Then the vacuum was turned on. The temperature of the external bath was maintained at 210-220°. The α-propylvinyl butyl ether was distilled off at 100-120° (180 mm). At the end of the reaction, the temperature of the external bath was brought up to 240°, and the vacuum was brought to 40 mm. The ether collected was washed with water and dried over potassium carbonate. On redistillation, the following fractions were obtained:

First, b. p. 25-26° (20 mm), n_D^{20} 1.4129, 1.6 g; 2nd, b. p. 56-60° (20 mm), n_D^{20} 1.4128, 47.5 g; 3rd, b. p. 60-105° (20 mm), n_D^{20} 1.4360, 1.2 g; 4th, b. p. 105-108° (20 mm), n_D^{20} 1.4468, 10.3 g. The residue was an oily brown product, 3.4 g.

After repeated distillation of the 2nd fraction over sodium, 41.5 g (65%) of the α-propylvinyl butyl ether was obtained. The methylpropyl ketone obtained by hydrolysis of the ether was characterized as the 2,4-dinitrophenylhydrazone with m. p. 144°. A mixed sample did not give any depression in melting point.

TABLE 1

Raman Spectra of Substituted Vinyl Butyl Ethers (cm^{-1})*

$CH_2=CH-OC_4H_9$	$CH_2=C(n\text{-}C_4H_9)-OC_4H_9$	$CH_2=C(iso\text{-}C_4H_9)-OC_4H_9$
912	—	421
940	—	549
959	748	637
980	802	796
1016	823	823
1027	850	844
1039	877	880
1085	910	908
1108	957	952
1129	1037	1030
1149	1066	1099
1185	1110	1118
1307	1130	1167
1321	1206	1226
1414	1234	1298
1435	1301	1335
1455	1347	1384
1468	1395	1403
1611	1450	1450
1638	1596	1591
1653	1654	1653

* Raman spectra were obtained by T. N. Shkurina.

By the method described above, other representatives of the α-substituted vinyl butyl ethers were prepared, the constants of which are given in Tables 3 and 4.

TABLE 2

Constants of β-Bromoalkyl Ethers*

Formulas and Names of Ethers	Boiling Point (pressure in mm)	Yield (in %)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Found % C	Found % H	Found % Br	Empirical Formula	Calculated (%) C	Calculated (%) H	Calculated (%) Br
$CH_2Br-CH(C_2H_5)-OC_4H_9$ α-Ethyl-β-bromoethyl butyl	80—81° (12)	88.6	1.4456	1.1556	48.24	48.62	45.87, 45.89	8.08, 8.09	37.98, 37.97	$C_8H_{17}OBr$	45.94	8.17	38.21
$CH_2Br-CH(C_3H_7)-OC_4H_9$ α-Propyl-β-bromoethyl butyl	91—92 (11)	77.2	1.4476	1.290	52.89	53.25	48.40, 48.57	8.41, 8.51	35.66, 35.95	$C_9H_{19}OBr$	48.43	8.50	35.87
$CH_2Br-CH(C_4H_9)-OC_4H_9$ α-Butyl-β-bromethyl butyl	114—115 (15)	72.2	1.4498	1.1041	57.77	57.88	50.28, 50.35	8.78, 8.81	33.55, 33.60	$C_{10}H_{21}OBr$	50.57	8.92	33.68
$CH_2Br-CH(iso-C_4H_9)-OC_4H_9$ α-Isobutyl-β-bromoethyl butyl	6.5—67.5 (18)	66.8	1.4482	1.1014	57.72	57.88	50.59, 50.72	8.81, 8.89	33.99, 33.70	$C_{10}H_{21}OBr$	50.57	8.92	33.68
$CH_2Br-CH(iso-C_5H_{11})-OC_4H_9$ α-Isoamyl-β-bromoethyl butyl	32—133 (20)	74.9	1.4500	1.0860	62.31	62.51	52.29, 52.44	9.52, 9.32	32.07, 31.99	$C_{11}H_{23}OBr$	52.59	9.23	31.81
$CH_2Br-CH(C_6H_5)-OC_4H_9$ α-Phenyl-β-bromoethyl butyl	144—145 (12)	58.5	1.5185	1.2219	63.88	63.60	55.96, 56.14	6.54, 6.70	31.33, 31.38	$C_{12}H_{17}OBr$	56.00	6.61	31.16

* All compounds were prepared for the first time.

TABLE 3

Conditions of Synthesis of α-Substituted Vinyl Butyl Ethers

Formulas and names of ethers	Temperature of external bath			Pressure (in mm)		B. P. of Substituted Ether on Dist.	Yield (in %)
	first 1.5–2 hours	after 2 hours	at end of reaction	separation time of ether	end of reaction		
$CH_2=C(C_2H_5)-OC_4H_9$ α-Ethylvinyl butyl	180—190°	210—215°	230°	—	190	130—140°	51.9
$CH_2=C(C_3H_7)-OC_4H_9$ α-Propylvinyl butyl	190—200	210—220	240	180	40	100—120	65.1
$CH_2=C(n\text{-}C_4H_9)-OC_4H_9$ α-n-Butylvinyl butyl	210—215	225—230	245	180	35	140—150	71.3
$CH_2=C(iso\text{-}C_4H_9)-OC_4H_9$ α-Isobutylvinyl butyl	200—210	220—225	240	180	40	120—130	60.6
$CH_2=C(iso\text{-}C_5H_{11})-OC_4H_9$ α-Isoamylvinyl butyl	185—195	210—215	240	185	35	150—160	70.4
$CH_2=C(C_6H_5)-OC_4H_9$ α-Phenylvinyl butyl	210—215	230—235	250	180	15	170—180	63.1

TABLE 4

Constants of α-Substituted Vinyl Butyl Ethers

Formulas and names of ethers	Boiling Point (Pressure in mm)	n_D^{20}	d_4^{20}	MR_D		Found %		Empirical Formula	Calculated %	
				found	calculated	C	H		C	H
$CH_2=C(C_2H_5)-OC_4H_9$ * α-Ethylvinyl butyl	53—54° (30)	1.4160	0.7977	40.34	40.47	74.97, 74.76	12.50, 12.62	$C_8H_{16}O$	74.97	12.58
$CH_2=C(C_3H_7)-OC_4H_9$ * α-Propylvinyl butyl	54—55.5 (15)	1.4218	0.8011	45.02	45.10	76.06, 76.00	12.68, 12.70	$C_9H_{18}O$	75.99	12.70
$CH_2=C(C_4H_3)-OC_4H_9$ ** α-Butylvinyl butyl	85—86 (20)	1.4238	0.8019	49.72	49.73	77.10, 77.15	12.76, 12.90	$C_{10}H_{20}O$	76.92	12.82
$CH_2=C(iso\text{-}C_4H_3)-OC_4H_9$ *** α-Isobutylvinyl but	71.5—73 (25)	1.4215	0.7968	49.65	49.73	77.10, 77.00	12.90, 12.95	$C_{10}H_{20}O$	76.92	12.82

* Prepared for the first time.

** Literature data: b. p. 177-178° (745 mm), n_D^{20} 1.4250, d_4^{20} 0.8025 [4].

*** Literature data: b. p. 166-168° (745 mm), n_D^{20} 1.4228, d_4^{20} 0.798 [4].

TABLE 4 (continued)

Formulas and names of ethers	Boiling Point (Pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Found % C	Found % H	Empirical Formula	Calculated % C	Calculated % H
$CH_2=C(iso\text{-}C_5H_{11})-OC_4H_9$ * α-Isoamylvinyl butyl	86.5—87° (18)	1.4256	0.8023	54.31	54.36	77.42, 77.42	12.91, 12.91	$C_{11}H_{22}O$	77.64	12.94
$CH_2=C(C_6H_5)-OC_4H_9$ * α-Phenylvinyl butyl	130.5—131.5 (22)	1.5186	0.9456	56.55	55.45	82.00, 81.95	9.06, 9.18	$C_{12}H_{16}O$	81.83	9.14

* Prepared for the first time.

SUMMARY

1. Six representatives of the α-bromoalkyl butyl ethers of the general formula $CH_2Br\text{-}CHR'\text{-}OC_4H_9$ have been synthesized and characterized, where R' = C_2H_5, C_3H_7, n-C_4H_9, iso-C_4H_9, iso-C_5H_{11}, and C_6H_5.

2. The corresponding α-alkyl(aryl)vinyl butyl ethers have been synthesized by splitting out hydrogen bromide from the β-bromalkyl butyl ethers.

3. It has been shown that the introduction of a radical in the α-position does not affect the frequency characteristic of the double bond.

LITERATURE CITED

[1] M. F. Shostakovskii, Simple Vinyl Ethers [in Russian](1952).

[2] M. F. Shostakovskii and Mageram Mamedov, Izvest. Akad. Nauk SSSR 1636 (1959).*

[3] A. N. Nesmeyanov, I. F. Lutsenko, and N. I. Vereshchagina, Izvest. Akad. Nauk SSSR 63 (1947).

[4] M. F. Shostakovskii and E. P. Gracheva, Zhur. Obshchei Khim. 23, 1320 (1953).*

[5] D. B. Killian, G. F. Hennion, and L. A. Neuwland, J. Am. Chem. Soc. 57, 544 (1935).

[6] A. E. Favorskii and M. N. Shchukina, Zhur. Obshchei Khim. 15, 385 (1945).

* Original Russian pagination. See C. B. translation.

INVESTIGATION IN THE FIELD OF SUBSTITUTED VINYL ETHERS

III. SYNTHESIS OF ALKOXYBROMOOLEFINS AND ALKOXYDIENES

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Translated from Zhurnal Obschei Khimii, Vol. 29, No. 12, pp. 3926-3930, December, 1959

Original article submitted November 20, 1958

Alkoxyhalobutenes $(CH_2XCH(OR)-CH=CH_2)$ and alkoxyhalopentenes $(CH_2X-CH(OR)-CH_2-CH=CH_2)$ belong to a class of compounds that has received little investigation. Having three reaction centers, these compounds are of great interest, especially from the point of view of polymerization and copolymerization.

Alkoxyhalobutenes were first prepared [1] by the reaction of alkoxyhypohalides with divinyl. They also can be prepared by the reaction of vinyl- or allylmagnesium bromides with α, β-dihalodialkyl ethers. Thus, ethoxybromopentene is obtained by the action of allylmagnesium bromide on α, β-dibromodiethyl ether [2].

The alkoxybromoolefins prepared by us (Table 1), by the reaction of vinyl- and allylmagnesium bromides with α, β-dibromodiethyl and α, β-dibromoethyl butyl ethers, were used for the synthesis of alkoxydienes (Table 2).

In the literature there are a number of reports relating mainly to 1-alkoxybutadienes-1,3. There has been comparatively little work on the synthesis of 2-alkoxybutadienes-1,3. 2-Alkoxybutadiene-1,3 was prepared for the first time [3] from 1,3,3-trialkoxybutane; later 2-ethoxybutadiene-1,3 was prepared by the condensation of vinylacetylene with ethyl alcohol [4]. 2-Ethoxy-and 2-butoxybutadiene-1,3 were prepared by splitting out hydrogen bromide from the corresponding alkoxybromoolefins [1]. There are no data relating to the synthesis of 2-alkoxypentadienes-1,4 in the literature.

In previous work [5] it has been shown that in splitting out hydrogen bromide from β-bromoalkyl ethers ($CH_2Br-CHR'-OR$) the lability of the bromine atom increases with an increase in the weight of the alkyl radical. It was of interest to ascertain the effect of the vinyl and allyl radicals in the α-position on the lability of the bromine atom in alkoxybromoolefins. Experiments showed that while a large excess of potassium hydroxide and a high temperature (200-250°) are required to split out hydrogen bromide from the β-bromoalkyl ethers, in the case of the alkoxybromoolefins, hydrogen bromide is split out by the action of a methanol solution of alkali at a lower temperature (80-90°). Consequently, the bromine atom in the alkoxybromoolefins is more labile than that in the β-bromoalkyl ethers.

EXPERIMENTAL

α, β-Dibromodiethyl and α, β-dibromoethyl butyl ethers were prepared by the bromination of vinyl ethyl and vinyl butyl ethers [6]. Vinyl bromide was synthesized by splitting out hydrogen bromide from 1,2-dibromoethane with methanolic alkali solution.

1-Bromo-2-ethoxybutene-3. Vinylmagnesium bromide was prepared by the following method [8]: to 12 g of Mg in 200 ml of tetrahydrofuran was added, drop by drop, 36 g of vinyl bromide. To the complex obtained there was added, at 20-25°, 90 g of α, β-dibromodiethyl ether diluted with an equal volume of dry ether. The reaction mixture was allowed to stand for 10-12 hours at room temperature. Decomposition was accomplished

TABLE 1

Formulas and names of alkoxybromoolefins	Boiling point (pressure in mm)	Yield (in %)	n^{20}_D	d^{20}_4	MR_D		Found %			Empirical Formula	Calculated %		
					found	calculated	C	H	Br		C	H	Br
$CH_2Br-CH(OC_2H_5)-CH=CH_2$ * 1-Bromo-2-ethoxybutene-3	51.2—52.5° (12)	57.4	1.4570	1.2641	38.52	38.89	40.42, 40.30	6.14, 6.25	44.73, 44.51	$C_6H_{11}OBr$	40.18	6.14	44.69
$CH_2Br-CH(OC_4H_9)-CH=CH_2$ ** 1-Bromo-2-butoxybutene-3	90—92 (20)	66.9	1.4566	1.1774	47.89	48.15	46.39, 46.45	7.32, 7.30	38.65, 38.67	$C_8H_{15}OBr$	46.39	7.30	38.58
$CH_2Br-CH(OC_2H_5)-CH_2-CH=CH_2$ *** 1-Bromo-2-ethoxypentene-4	71—72 (20)	58.4	1.4590	1.2262	43.06	43.52	43.45, 43.43	6.74, 6.73	41.26, 41.24	$C_7H_{13}OBr$	43.54	6.77	41.38
$CH_2Br-CH(OC_4H_9)-CH_2-CH=CH_2$ 1-Bromo-2-butoxypentene-4	104—105 (23)	68.2	1.4595	1.1513	52.57	52.78	48.82, 48.90	7.76, 7.62	35.92, 36.13	$C_9H_{17}OBr$	48.88	7.74	36.13

*B.p. 153.5—154.2°, n_D^{20} 1.4595, d_4^{20} 1.2611 [1]; b.p. 50° (15 mm), n_D^{20} 1.4565, d_4^{20} 1.256 [7].
**B.p. 73.5-74° (10 mm), n_D^{20} 1.4590, d_4^{25} 1.1756 [1].
***B.p. 69—71° (21 mm), n_D^{20} 1.4592, d_4^{20} 1.255 [2].

with 10% acetic acid solution at 20° (the flask was cooled with ice water). The aqueous layer, after separation from the ether layer, was extracted twice with ether and dried over calcium chloride. The mixture of ether and tetrahydrofuran was distilled off on a water bath. The residue was distilled in vacuo. The following fractions were obtained:

1st, b.p. 25–49° (28-12 mm), n_D^{20} 1.4550, 1.3 g; 2nd, b.p. 50–54° (12 mm), n_D^{20} 1.4580, 48.4 g; 3rd, b.p. 54–60° (12 mm), n_D^{20} 1.4590, 1.6 g; residue 3.1 g.

After repeated distillation of the 2nd fraction, 46.1 g of 1-bromo-2-ethoxybutene-3 was obtained.

1-Bromo-2-ethoxybutene-3 was prepared in a similar manner. The constants of the compounds are given in Table 1.

1-Bromo-2-ethoxypentene-4. Fifty grams of α, β-dibromodiethyl ether was added dropwise, at 50°, to the allylmagnesium bromide prepared from 6 g of Mg and 35 g of allyl bromide. The reaction was further carried out as described previously [5]. After the ether was distilled off, the residue was distilled in vacuo. The following fractions were obtained:

1st, b.p. 70–74° (22 mm), 0.38 g; 2nd, b.p. 74–78° (22 mm), n_D^{20} 1.4586, 52.8 g; residue 3.6 g.

After repeated distillation of the 2nd fraction, 48.6 g of 1-bromo-2-ethoxypentene was obtained. 1-Bromo-2-butoxypentene-4 was prepared by the same method. The constants of the compounds are given in Table 2.

2-Ethoxybutadiene-1,3. Fifty grams of 1-bromo-2-ethoxybutene-3 and 25 g of pulverized potassium hydroxide in 50 ml of methanol were placed in a copper flask equipped with a stirrer and a reflux condenser. The mixture was heated at 80–90° for 3 hours. Then, when the temperature had reached 30°, the reflux condenser was replaced with a herringbone dephlegmator and the alkoxybutadiene was distilled off together with the methanol. The product obtained was diluted with water. The upper ether layer was dried over potassium carbonate. After 2 distillations, 20.5 g of 2-ethoxybutadiene-1,3 was obtained. Other representatives of the 2-alkoxydienes, the constants of which are given in Table 2, were prepared in a similar manner.

TABLE 2

Formulas and names of alkoxydienes	Boiling point (pressure in mm)	Yield %	n^{20}_D	d^{20}_4	MR_D found	MR_D calculated	Found % C	Found % H	Empirical formula	Calculated % C	Calculated % H
$CH_2=C(OC_2H_5)-CH=CH_2$ * 2-Ethoxybutadiene-1,3	93–95°	65.8	1.4382	0.8138	31.67	30.74	73.44, 73.51	10.10, 10.20	$C_6H_{10}O$	73.43	10.27
$CH_2=C(OC_4H_9)-CH=CH_2$ ** 2-Butoxybutadiene-1,3	63–65 (40)	71.3	1.4415	0.8092	41.12	39.84	76.15, 76.29	11.20, 11.30	$C_8H_{14}O$	76.13	11.18
$CH_2=C(OC_2H_5)-CH_2-CH=CH_2$ 2-Ethoxypentadiene-1,4	107–108	70.7	1.4202	0.8177	35.11	35.23	74.80, 75.08	10.76, 10.87	$C_7H_{12}O$	74.76	10.78
$CH_2=C(OC_4H_9)-CH_2-CH=CH_2$ 2-Butoxypentadiene-1,4	71.5–72.5 (18)	77.9	1.4615	0.8333	44.47	44.63	76.92, 76.97	11.44, 11.47	$C_9H_{16}O$	77.08	11.50

*B.p. 93-94°, n_D^{20} 1.4450, d_4^{20} 0.8177 [1]; b.p. 96.5°, n_D^{20} 1.4401, d_4^{20} 0.8153 [3]; b.p. 113-117°, n_D^{20} 1.430, d_4^{20} 0.8390 [4].

**B.p. 64-65° (54mm), n_D^{20} 1.4450, d_4^{20} 0.8192 [1]; b.p. 65° (54mm), n_D^{20} 1.4415, d_4^{20} 0.8223 [3].

SUMMARY

1. The following compounds were synthesized: 1-bromo-2-ethoxy- and 1-bromo-2-butoxybutene-3; 1-bromo-2-ethoxy- and 1-bromo-2-butoxypentene-4.

2. It has been shown that the bromine atom in the alkoxybromoolefins is more labile than that in the β-bromoalkyl ethers.

3. By splitting out hydrogen bromide from alkylbromoolefins, the following alkoxydienes were prepared: 2-ethoxy- and 2-butoxybutadiene-1,3; 2-ethoxy- and 2-butoxypentadiene-1,4.

LITERATURE CITED

[1] A. A. Petrov, Zhur. Obshchei Khim. 8, 208 (1938).

[2] H. Sholmaker and C. E. Boord, J. Am. Chem. Soc. 53, 1505 (1931).

[3] H. B. Dykstra, J. Am. Chem. Soc. 57, 2255 (1935); R. O. Norrish, L. J. Verbanc and G. F. Hennion, J. Am. Chem. Soc. 60, 1159 (1938).

[4] I. A. Rottenberg and M. A. Favorskii, Zhur. Obshchei Khim. 6, 185 (1936).

[5] M. F. Shostakovskii and Mageram Mamedov, Izvest. Akad. Nauk SSSR 1636 (1959);* Zhur. Obshchei Khim. 29, 3922 (1959).*

[6] A. E. Favorskii and M. N. Shchukina, Zhur. Obshchei Khim. 15, 1320 (1945).

[7] H. Normant and G. Martin, Bull Soc. Chim. 429 (1957).

[8] H. Normant, Compt. rend. 239 (1954).

*Original Russian pagination. See C. B. translation.

PREPARATION OF 2- AND 4-STYRYL DERIVATIVES OF QUINOLINE USING BENZYLIDENANILINE

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Translated from Zhurnal Obschei Khimii, Vol. 29, No. 12, pp. 3930-3934, December, 1959

Original article submitted December 10, 1958

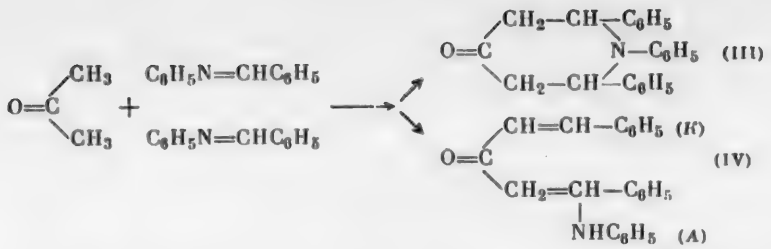
In an investigation carried out by us on the absorption spectra of molecular complexes of quinoline and styrylquinoline compounds with aromatic amines [1], we had to synthesize 2-styrylquinoline (2SQ) and 4-styrylquinoline (4SQ). When the synthesis of 4SQ was carried out as described in the literature, we did not obtain satisfactory results. We were able to find a good method for the synthesis of 4SQ, using benzylidenaniline in the presence of acetic anhydride in place of benzaldehyde for the condensation with lepidine. This method gave excellent results also in the synthesis of 2SQ and a number of other similar compounds.

Doebner and Miller [2] described the preparation of 4SQ by heating equal amounts of lepidine and benzaldehyde in the presence of zinc chloride for many hours in a tube at 180°. These authors obtained 4SQ as well-formed crystals, but did not indicate the yield. The synthesis was repeated later with a yield of 56.5% [3]. In spite of repeated attempts, we did not succeed in obtaining 4SQ by this method in satisfactory quality and yield. All attempts to prepare 4SQ by the condensation of the starting materials mentioned in the presence of other catalysts (hydrochloric acid, acetic anhydride, and piperidine) gave negative results. These failures forced us to seek other modes of synthesis.

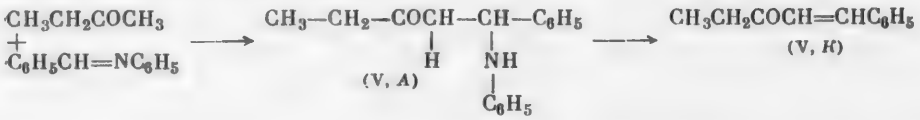
As is well known, the hydrogen atoms of the methyl group in quinaldine and lepidine are in an activated state because of the influence of the electron-accepting azomethine group of the heterocycle $-\overset{\circ-}{N}=\overset{\circ+}{C}<$. This effect is similar to the activating effect of the carbonyl on the H atom on the α-C atom of aldehydes and ketones, and apparently the condensation reactions of 2- and 4-methylquinolines have much in common with aldol and crotonic condensation. This analogy is confirmed by the observation that when quinaldine is condensed with benzaldehyde, not only 2SQ may be obtained, but also an intermediate compound of the aldol type, phenylquinaldylcarbinol (I) (when the condensation is brought about by the action of light).

When the carbinol (I) is boiled for three hours with acetic anhydride, it goes over to 2SQ (II) [4] in a manner similar to the transformation of aldol to crotonaldehyde.

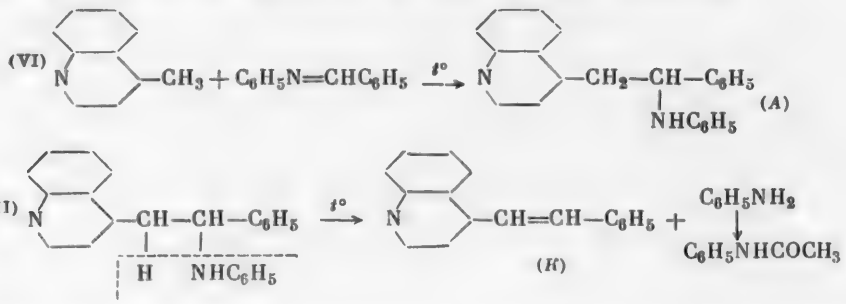
We turned out attention to the fact that the methyl groups of acetone are capable of reacting not only with benzaldehyde, but with benzylidenaniline. In this process, in addition to the main reaction product, 1,2,6-triphenylpiperidone-4 (III), the unsaturated compound β-anilino-β-phenylethyl styryl ketone (IV) also is formed [5,6].



The formation of a group analogous to the aldol grouping (A) is the result of the addition of an active CH_3-group to the benzylidenaniline. The formation of compounds with such a grouping as (A) has also been observed for ketones of the structure CH_3COCH_2R. Thus, when benzylidenaniline was reacted with methyl ethyl ketone, ethyl β-anilino-β-phenylethyl ketone (V,A) was produced.



It might be expected that the grouping (V,A) under properly selected conditions (for example, heating in acetic anhydride) would be further converted to the grouping (V,K), similar to the grouping in crotonaldehyde. The correctness of this assumption is confirmed by the presence of the system K also in compound (IV). Hence, the thought occurred to us to investigate the reaction of lepidine with benzylidenaniline.



Taking into account that this reaction should proceed in two stages, A (VI) and K (VII), by analogy with the crotonic condensation, we carried out the reaction in acetic anhydride medium to tie up the aniline formed.

This supposition proved to be correct. Actually, this reaction goes even when the starting materials are simply heated in the absence of any condensing agents, but with a yield of not more than 20%. In the presence of acetic anhydride, the yield could be increased to 67%. On the basis of the considerable increase in yield observed when the reaction is carried out in the presence of acetic anhydride, it can be assumed that reactions (VI) and (VII) have somewhat of an equilibrium character.

The usual method of preparing 2-styrylquinoline is by heating quialdine with benzaldehyde in the presence of an acid catalyst (zinc chloride, acetic anhydride, or hydrochloric acid) [7—9, 3]. To avoid the formation in this process of a small amount of diquinaldinic compound, it has been recommended that the reaction be carried out with an excess of benzaldehyde. The part played in this condensation by zinc chloride or other catalysts of an acid nature has been explained by a reaction mechanism with coordinate addition of a molecule of zinc chloride to the nitrogen of the heterocycle [10]. •

The condensation of quinaldine with benzaldehyde may proceed, however, without the participation of an acid catalyst, as our experiments have shown, and specifically in the presence of a basic catalyst, piperidine, with a 70% yield. This method gives better results than the method using zinc chloride. However, we obtained the

• This mechanism basically conforms with the mechanism proposed by Mills for the condensation of naphthoquinaldine iodoethylate with p-dimethylaminobenzaldehyde in the presence of a basic catalyst, piperidine [11].

best results here also by using benzylidenaniline in the presence of acetic anhydride in place of benzaldehyde. The reaction was completed in a few minutes with a yield of up to 80%.

EXPERIMENTAL

1. Preparation of 2-styrylquinoline (2SQ) by the condensation of quinaldine with benzaldehyde. - a) Reaction in the presence of piperidine. A mixture of 7.15 g (0.05 mole) of quinaldine, 5.36 g (0.05 mole) of well-purified benzaldehyde, and 10 drops of piperidine was heated in a round-bottomed flask with a reflux condenser at 150° for 10 hours. The brownish-yellow crystalline mass that was formed was mixed with a small amount of alcohol, filtered off, and washed on the filter twice with alcohol. This treatment removed the brownish coloration from the crystals, and a light yellow product remained on the filter. After two crystallizations from alcohol, light yellow (almost colorless) needles were obtained. M.p. 99° (99—100° [12]). Yield 70%. The 2SQ obtained was converted to the corresponding iodoethylate by heating with ethyl iodide. The product was analyzed for iodine by the Stepanov method.

Found %: I 32.93. $C_{19}H_{18}NI$ Calculated %: I 32.79.

b) Reaction in the presence of zinc chloride. A reaction mixture of 2,86 g (0.02 mole) of quinaldine, 2.12 g (0.02 mole) of benzaldehyde, and 2 g of zinc chloride was heated in a round-bottomed flask at 120° for 2 hours. The contents of the flask solidified. The color was dark brown. Water was added to the flask and it was heated to dissolve the zinc chloride. The contents of the flask separated into layers. Upon cooling, the lower layer solidified and was filtered off. After a second crystallization from alcohol, crystals of a yellowish color were obtained, with m.p. 96.5—98°. Yield 1.65 g (35%). Another 1.09 g of 2SQ was isolated from the alcoholic mother liquors. Total yield ~ 60%. When the heating period was shortened to 0.5 hour, the yield was only 8.1%.

2. Preparation of 2-styrylquinoline by the condensation of quinaldine with benzylidenaniline. a) Condensation in acetic anhydride medium. A mixture of 14.3 g (0.1 mole) of quinaldine, 21.8 g (0.1 mole + 20% excess) of benzylidenaniline, and 20.4 g (0.2 mole) of acetic anhydride was slowly heated in a round-bottomed flask equipped with a thermometer (immersed in the reaction mixture) and a reflux air-cooled condenser. At 146° slight boiling occurred in the flask and rapidly intensified, and the temperature rose to 156—158°. This temperature was maintained for 5 minutes, after which a decrease to 154° was observed, indicating the end of the reaction. The warm mass was poured, with vigorous stirring, into a beaker containing 250 ml of cold water. A dark-brown oily liquid collected on the bottom of the beaker and solidified on cooling. The stratified mixture was not separated, but sodium carbonate solution was added to it carefully until there was an alkaline reaction to phenolphthalein. After vigorous stirrring, the oil on the bottom of the beaker solidified on cooling. The precipitate was transferred to a porcelain dish, coalesced under water, and washed several times by decantation with warm water. The 2SQ obtained was further purified. For this purpose, the base was dissolved in dilute hydrochloric acid, avoiding a large excess. The solution of the 2SQ hydrochloride was filtered through a folded filter and the base was again separated with sodium carbonate solution (test with phenolphthalein). The precipitate was filtered off, transferred to a porcelain dish, and coalesced in it 2—3 times under water, with a change of water each time. Then it was washed several times with warm water by decantation and filtered. The ground and air-dried product had a slight yellow color and m.p. 99.5°. Yield 18.16 g (78.7%) The 2SQ obtained by this method was identified by a mixed melting point determination with a sample obtained by condensation with benzaldehyde in the presence of piperidine (see above). No depression in melting point was observed. When the condensation of quinaldine with benzylidenaniline was carried out in the absence of acetic anhydride, a lower yield was obtained. We will describe two experiments.

b) Condensation in butyl alcohol medium. 4.29 g of quinaldine (0.03 mole), 5.43 g of benzylidenaniline, and 5 ml of butyl alcohol were heated, in the same apparatus as previously described, to gentle boiling for 68 hours. The temperature of the reaction mixture at first was 135°; at the end it was elevated to 160°. After the reaction mass had cooled, an equal volume of alcohol was added to it. After the flask was heated for a short time and cooled, a precipitate separated out, which was filtered off and washed on the filter with a small amount of alcohol. The air-dried product had a yellowish color. M.p. 97—98°. Weight 2.85 g (41.3%). An additional 0.9 g of more contaminated 2SQ was obtained from the mother liquor. Total yield about 54.3%.

c) Condensation without addition of solvent. A mixture of 10.01 g (0.07 mole) of quinaldine and 12.67 g (0.07 mole) of benzylidenaniline was heated for 5 hours at 195°. Upon cooling, the mass partially crystallized.

The crystals were filtered off and washed on the filter 3 times with a small amount of ether. The air-dried product had a yellowish color. M.p. 95—96 .5°. Weight 6.45 g. By addition of sulfuric acid to the mother liquor, a sulfate was obtained from which another 2.05 g was recovered. Total yield 8.5 g, or 52%, calculated on the purified product.

3. Preparation of 4-styrylquinoline (4SQ) by condensation of lepidine with benzylidenaniline. a) Condensation without addition of acetic anhydride. In a round-bottomed flask equipped with a reflux air-cooled condenser were mixed 6.09 g (0.0338 mole) of benzylidenaniline and 4.83 g (0.0338 mole) of lepidine. When the materials were mixed, a drop in temperature to +5° was observed. The reaction mixture was heated on an oil bath at 200—210° for 24.5 hours. After the mixture had been cooled, 15% hydrochloric acid was added to the dark-brown oily liquid that was formed, until there was an acid reaction to methyl orange. Upon cooling with water, the reaction mass solidified. The yellow precipitate of 4SQ hydrochloride was filtered off and washed twice on the filter with ether and then dissolved in hot water (yellow solution). Sodium carbonate solution was added to the cooled solution of the hydrochloride until there was an alkaline reaction to phenolphthalein. The base precipitated as an oily gray-yellowish mass that solidified upon standing. By recrystallization from 70% alcohol, fine, regular, transparent crystals were obtained in the form of right-angled parallelopipeds that sparkled in the light. M.p. 90.5—91.5° (92° [2]). Weight 1.5 g (19.2%). Upon standing, the crystals lost their transparency and became cloudy. Another 0.12 g of the base was obtained from the acid filtrate after the 4SQ hydrochloride had been filtered off. Total weight of crystals obtained 1.62 g (20.7%). After a second crystallization, m.p. 91.5—92°. Fusion slightly yellowish.

When the time of heating was shortened to 7 hours, the yield of 4SQ decreased to 10%. M.p. 92—92.5°.

Found %: N 6.00, 6.26; C 87.92, 87.70; H 6.22, 6.26. $C_{17}H_{13}N$. Calculated %: N 6.06; C 88.27; H 5.67.

b) Condensation in the presence of acetic anhydride. A mixture of 7.15 g (0.05 mole) of lepidine, 13.72 g (0.096 mole) of benzylidenaniline, and 33 moles of acetic anhydride was heated to boiling (140°) in a round-bottomed flask equipped with a reflux air-cooled condenser and thermometer, for 30 hours. The contents of the flask was poured into a beaker containing 175 ml of water. After thorough mixing, a solution of sodium carbonate was added to the mixture until there was a weak alkaline reaction to phenolphthalein. The liquid stratified. On the bottom of the flask there was a yellowish-brown oily liquid. The aqueous layer was carefully decanted, and 10% hydrochloric acid was added to the oil (after it had been washed twice by decantation) until there was a strongly acid reaction. The yellow precipitate of 4SQ hydrochloride that had separated out was filtered off, washed on the filter with alcohol and with ether, and then dissolved in hot water. The solution was not homogeneous: a dark-brown layer floated on the top (benzaldehyde odor). When the hot solution was filtered, the oil solidified on the filter. After the filtrate had cooled, dry sodium carbonate was added to it (until there was a reaction to phenolphthalein) and the precipitate of base that separated out was filtered off. After crystallization from alcohol, 6.06 g of well-formed crystals were obtained. M.p. 90.5—91°. To obtain an additional amount of the base, concentrated HCl was added to the alcoholic filtrate, and the precipitate of salt that separated was washed on the filter with alcohol and ether and then converted to the base as indicated above. In this way, an additional 1.72 g of crystals were obtained with m.p. 90.5—91°. Total yield of 4SQ 7.78 g (67.4%). After two crystallizations from alcohol, m.p. 91—92°. The 4SQ obtained in this experiment was identified by determining the melting point of a sample mixed with an analyzed specimen. No depression was observed. When the time of heating was shortened to 12 hours, the yield of 4SQ decreased to 30%.

SUMMARY

1. A method has been proposed for the preparation of 4-styrylquinoline in 67% yield by heating lepidine with benzylidenaniline in acetic anhydride for many hours. In the absence of acetic anhydride the yield of 4-styrylquinoline was only about 21%.

2. The condensation of benzylidenaniline with quinaldine in acetic anhydride at 150—160° is completed in a few minutes with a 78% yield of 2-styrylquinoline.

LITERATURE CITED

[1] V. A. Izmail'skii and P. A. Solodkov, Doklady Akad. Nauk SSSR. 60, 587 (1948); 75, 391, (1950); 91, 11, 19 (1953).

[2] O. Doebner and W. Miller, Ber. 18, 1640 (1885).

[3] C. Kaslow and R. Stayner, J. Am. Chem. Soc. 67, 1716 (1945).

[4] A. Benrath, J. pr. Chem. (2) 73, 386 (1906).

[5] C. Mayer, Bull Soc. Chim. (3), 31, 953 (1904); (4), 19, 454 (1916).

[6] Petrenko-Kritschenko, Ber. 42, 3694 (1909).

[7] Wallach, Ber. 16, 2008 (1883).

[8] Jacobsen and Reimer, Ber. 16, 2607 (1883).

[9] E. Noelting and E. Witte, Ber. 39, 2750 (1906).

[10] Taylor and Baker in Sidgwick's Organic Chemistry of Nitrogen (Oxford University Press, 1937) p. 557.

[11] W. H. Mills and R. Raper, J. Chem. Soc. 127, 2474 (1925).

[12] Izmail'skii, J. pr. Chem. 85, 91 (1912).

CONTRA POLARIZED SYSTEMS AND SPECTRA

V. THE COLOR OF SOME DERIVATIVES OF 4'-NITRO-4-AMINOBENZANILIDE CONTAINING ADDITIONAL METHYL AND METHOXY GROUPS IN THE ANILIDE RING

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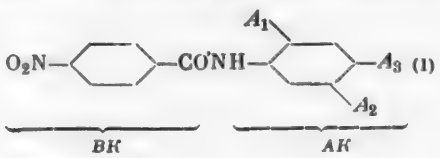
Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3935–3943, December 1959

Original article submitted December 25, 1958

I. In a previous communication [1] we discussed the phenomenon of color for 4'-nitrobenzanilides of structure (I).



where A_1, A_2 and A_3 are electron-donor groups. Based on visual observations, and also on spectral studies (absorption and reflection spectra), it was established that the introduction of an additional donor group A_2 (CH_3 or OCH_3) in the anilide moiety para to the first group A = OCH_3, when compared with derivatives containing only one OCH_3 group, causes a deepening of the color. This was explained by an increase in the electron-donor properties of the system AK due to the formation of a contra polarized system as a result of the two donors in the para-position reacting with each other. These conclusions were confirmed later [2].

In this communication we discuss the effect on the color when the additional groups $A_1 = CH_3$ and $A_2 = OCH_3$ are introduced into those 4'-nitro derivatives of benzanilide (I) that contain either NH_2 or $NHCOCH_3$ as the A_3 group. Compound No. 1 with the $NHCOCH_3$ group para to the NH group (I, A_1 and A_2 = H, $A_3 = NHCOCH_3$) has a light lemon-yellow color. The additional introduction into compound No. 1 of the two electron-donor groups CH_3 and OCH_3 para to each other [No. 2, Table 1 (I, $A_1 = CH_3$, $A_2 = OCH_3$, $A_3 = NHCOCH_3$] has hardly any effect on the color. However, in the reflection spectra [3] (or, as was proposed by us recently, in the absorption spectra of a powder surface [2]), obtained using a Beckman spectrophotometer, for compounds containing $A_3 = NHCOCH_3$, along with the additional groups $A_1 + CH_3$ and $A_2 = OCH_3$, a distinct hypsochromic shift was observed instead of the bathochromic shift expected by us on the basis of the results obtained in an earlier investigation [1] (Fig. 1, 1 and 2). We will mention that the percent of light absorption (% E) at 420 mμ was somewhat greater for No. 2 than for No. 1, since after the intersection of the curves at around 440 mμ the % E in the longer wavelength region was always lower for No. 2.

The visual color of the 4-amino compound No. 4 containing the additional groups $A_1 = CH_3$ and $A_2 = OCH_3$ (Table 1), was a deeper blue (bordeaux) than that of the starting 4-NH_2 compound No. 3 (dark-orange color), but in the powder the color difference proved to be less: red-orange and orange. However, the curves of the reflection spectra (% R) [3], or of the absorption spectra of the powder surface, obtained using a Beckman spectrophotometer, also showed an unexpected distinct hypsochromic effect (Fig. 1, 3 and 4).

TABLE 1

Color of 4-Nitrobenzanilide Derivatives of Structure (I)

No. of compound	Substituting donor chromophores in (I)			Color in crystals	Reflection spectra • • (% R) for λ (in mμ)							
	A_1	A_2	A_3			400	420	440	460	480	600	640	700
1	H	H	$NHCOCH_3$	Lemon-yellow	a —	6.0	7.8	14.1	29.5	77.0	80.8	82.3
					b 9.5	10.0	13.5	23.3	42.0	73.0	82.5	84.5
2	CH_3	OCH_3	$NHCOCH_3$	Lemon-yellow	a —	5.2	8.8	17.9	37.4	86.2	86.7	87.1
					b 4.0	4.5	8.5	19.0	40.2	88.0	89.0	89.5
3	H	H	NH_2	Dark orange •	a —	2.8	3.0	3.1	3.7	30.5	50.0	67.3
					b 3.0	3.0	3.4	4.0	5.5	54.0	71.5	82.2
4	CH_3	OCH_3	NH_2	Dark bordeaux •	a —	4.5	5.0	5.6	6.5	39.9	70.6	83.8
					b 5.4	4.95	5.7	6.5	7.5	47.5	77.0	87.8

•In powder form No. 4 is orange, and No. 5 is red-orange.

• •The values obtained using a Beckman spectrophotometer are designated by a, and those using a Hardy spectrophotometer are designated by b.

TABLE 2

Absorption Spectra of 4-NO_2-benzanilides of Structure (I), Containing Donor Group NH_2 or $NHCOCH_3$, c 10^{-4}, in Alcohol

No. of compound	A_1	A_2	A_3	λ_{max} (in mμ)		ϵ_{max}		Limit of absorption at ε	
				I (β)	II (α)	I (β)	II (α)	2000	1000
1	H	H	$NHCOCH_3$	262	~310	25400	7950	392	408
2	CH_3	OCH_3	$NHCOCH_3$	260	~315—320	20600	~5000	364	384
3	H	H	NH_2	260	357	19500	4650	422	446
4	CH_3	OCH_3	NH_2	256	355	17800	2080	330	408

In the 420—500 mμ region, the curve of methyl methoxy compound No. 4 (I, $A_1 = CH_3$, $A_2 = OCH_3$, $A_3 = NH_2$) lies below that of compound No. 3, containing only the NH_2 group, while at longer wavelengths (above 500 mμ), the curve of compound No. 4 shows a sharp hypsochromic shift when compared with the curve of p-NH_2 compound No. 3 (I, $A_1 = A_2 = H$, $A_3 = NH_2$). These results required verification and we repeated our investigation of the sbsorption spectra of the above indicated compounds (taken in powder form) using an automatically recording Hardy spectrophotometer Fig. 2).

A comparison of the curves in Figs. 1 and 2 (compare a and b in Table 1) also possesses interest for characterizing the effect of the accuracy of the instruments on the measurement results. We are of the opinion that the curves in Fig. 2 give us a more accurate characterization of the color of the compared compounds in the solid state. For both instruments the shape of the curves for compounds Nos. 1 and 2, having the p-$NHCOCH_3$ group in their molecule, proved to be quite similar only in the 500—700 mμ region, and also specifically when the two donors CH_3 and OCH_3 are introduced we can also detect a heightening of the color (Fig. 2). However, in contrast to Fig. 1, curves 1 and 2 in Fig. 2 intersect at 485 mμ, and in the region of maximum absorption 400—500 mμ, in contrast to the earlier measurement result (Fig. 1), we observed a deepening of the color when the two donors CH_3 and OCH_3 were introduced in contra position, expressed in a bathochromic shift of the curves and in an increase in the intensity of absorption, as we had expected on the basis of the results obtained in [1].

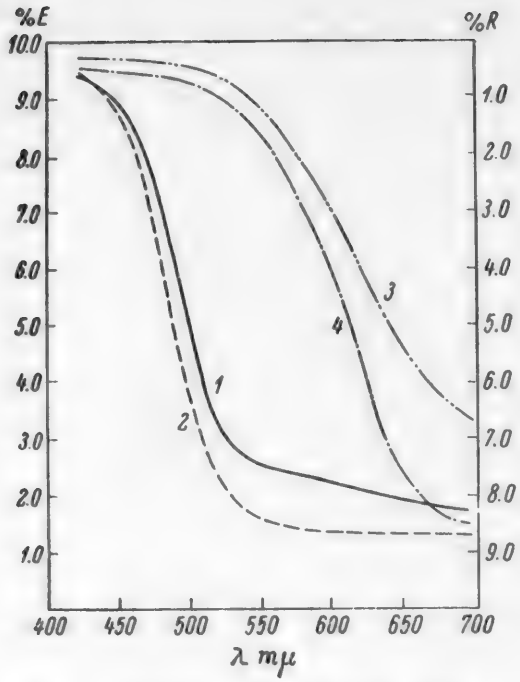


Fig. 1. Absorption spectra of powder surface of 4'-nitrobenzanilide derivatives (I), obtained using a Beckman spectrophotometer. The curve numbers correspond to the numbers of the compounds in Table 1. 1) 3-$NHCOCH_3$; 2) 2-CH_3; 5-OCH_3, 3-$NHCOCH_3$; 3) 3-NH_2; 4)3-CH_3, 5-OCH_3, 3-NH_2.

The curves for the compounds containing the p-NH_2 group, namely Nos. 3 and 4 in Fig. 2, are sharply different from the curves in Fig. 1. The pattern obtained here is somewhat similar to that described above for compounds Nos. 1 and 2 with the p-$NHCOCH_3$ group. Curves 3 and 4 (Fig. 2) intersect at about 538 mμ, and then again at about 614 mμ. In both the 400-530 mμ and 620-700 mμ regions, the introduction of the two donors CH_3 and OCH_3 caused a bathochromic shift of the curve; with the CH_3 and OCH_3 groups present we observed a close course of the two curves in the 538-614 mμ region, with a slight hypsochromic shift.

As a result, a reinvestigation of the absorption spectra of powder surfaces in the region of maximum absorption for the p-amino and p-acetamino derivatives revealed that introducing the two additional donors 2-CH_3 and 5-OCH_3 gives a hyperchromic and bathochromic shifts in the region of maximum absorption around 400—450 mμ, the same as we had expected. However, a hypsochromic effect is observed in the longer wavelength region, the same as in the first measurement.

II. To determine whether the above indicated effects are the result of exomolecular interactions or whether they are associated only with the endomolecular interactions of systems AK and BK, we undertook a study of the absorption spectra of compounds Nos. 1—4 in solution (Fig. 3). All of the compounds have two absorption bands: an intense band in the short-wave region, which we have designated by I (or β by a different designation), and a band of weak intensity in the long-wave region, which we have designated by II (or α). For compounds Nos. 1 and 2, band II shows only an inflection at about 310 mμ, whereas compounds Nos. 3 and 4 both show a maximum (especially well defined for compound No. 3) (Fig. 3, Table 2).

a) Comparing the absorption curves of compounds Nos. 1 and 2, each having a p-CH_3 CONH group (Table 2, Fig. 3), we see that for compound No. 2, having the groups 2-CH_3 and 5-OCH_3, ϵ for both bands I and II is low when compared with compound No. 1, while the entire long-wave portion of the spectral curve is shifted hypsochromically.* Taking into further consideration also the position of the absorption limits at $\epsilon = 2000$ ($\Delta\lambda = -18$ mμ) and 1000 ($\Delta\lambda = -24$ mμ), we can establish that in the given case the introduction of the 2-CH_3 and 5-OCH_3 groups caused a distinct hypsochromic effect.

b) A comparison of the absorption curves of compounds Nos. 3 and 4, containing the p-NH_2 group, gave an analogous but even more distinct picture. Here also the introduction of the 2-CH_3 and 5-OCH_3 groups caused ϵ_{max} for both of the bands of compound No. 4 to decrease ($\Delta\epsilon^{I}_{max} = -1700$, $\Delta\epsilon^{II}_{max} = -2570$). The long-wave portion for compound No. 4, containing the additional groups, lies considerably lower and is shifted hypsochromically when compared with No. 3 ($\Delta\lambda^{I}_{max} = -3$ mμ, and in the long-wave region $\Delta\lambda^{II}_{max} = -2$ mμ). An even sharper hypsochromic shift as the result of introducing additional donor groups emerges when a comparison is made of the absorption limits at $\epsilon = 2000$ ($\Delta\lambda = -82$ mμ) and $\epsilon = 1000$ ($\Delta\lambda = -38$ mμ). As a result, also for compounds with p-NH_2 groups, the introduction of the two additional donor groups CH_3 and OCH_3 caused a hypsochromic effect.

*The hypsochromic shift $\Delta\lambda^{I}_{max} = -2$ lies within the limits of measurement accuracy, whereas $\Delta\lambda^{II}_{max}$ cannot be determined accurately, since the long-wave band appears only in the form of inflections (which is designated in Table 2 by the sign ~).

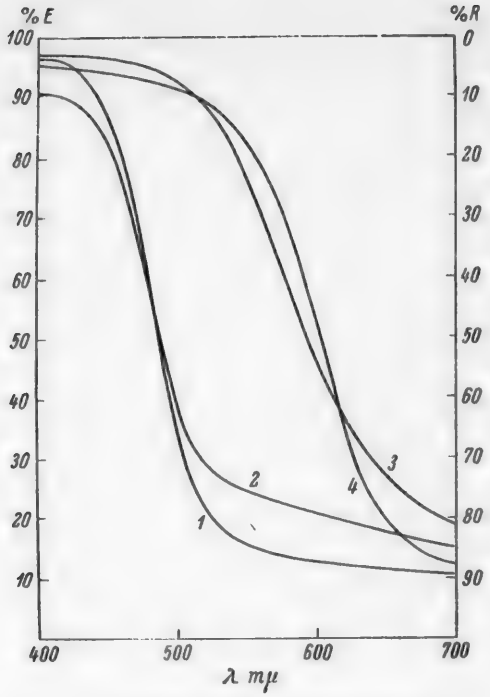


Fig. 2. Absorption spectra of powder surface of 4'-nitrobenzanilide derivatives (I), obtained using a Hardy spectrophotometer. The curve numbers correspond to the numbers of the compounds in Table 1.

The curve designations are the same as in Fig. 1.

c) A comparison of the compounds containing $NHCOCH_3$ and NH_2 groups (Nos. 1 and 3, and 2 and 4) reveals that in both cases replacing the $NHCOCH_3$ by the NH_2 group causes a decrease in λ_{max} of the short-wave band I. In the long-wave region (λ^{II}_{max}) for compounds Nos. 1 and 3, without the additional donor groups CH_3 and OCH_3, replacing the $NHCOCH_3$ group by the NH_2 group caused a bathochromic shift of the curve with some decrease in ϵ^{II}_{max} in the region of the maximum. For compounds Nos. 2 and 4, containing the additional groups, the curves in the region of λ^{II}_{max} lie very close to each other and do not show a well expressed maximum.

As a result, an investigation of absorption spectra in alcohol solution confirmed the fact that when $NHCOCH_3$ and NH_2 groups are present in the para position, the introduction of the two additional electron-donor groups 2-OCH_3 and 5-CH_3 in the same ring causes a hypsochromic effect, and the arrangement of the spectral curves in solution is the same as for the compounds in powder form. From this it is possible to conclude that the indicated hypsochromic effect in the solid state is the consequence of endomolecular interactions.

A hypsochromic shift in the long-wave portion is more pronounced when the p-NH_2 group is present than when the p-$NHCOCH_3$ group is present. This observation indicates that the hypsochromic effect is enhanced when the donor properties rise. It is possible to offer the theory that it is due to a reduction in the donor properties of the contra system A_1—A_2 and of the entire system AK as a whole due to the reaction of A_3 with other groups. Further studies are needed to explain the mechanism of this reaction. To some degree, a similar hypsochromic influence of an additional electron-donor group when introduced meta to a second donor group (NH_2) was observed earlier for 2, 4-dinitrodiphenylamine derivatives [5].

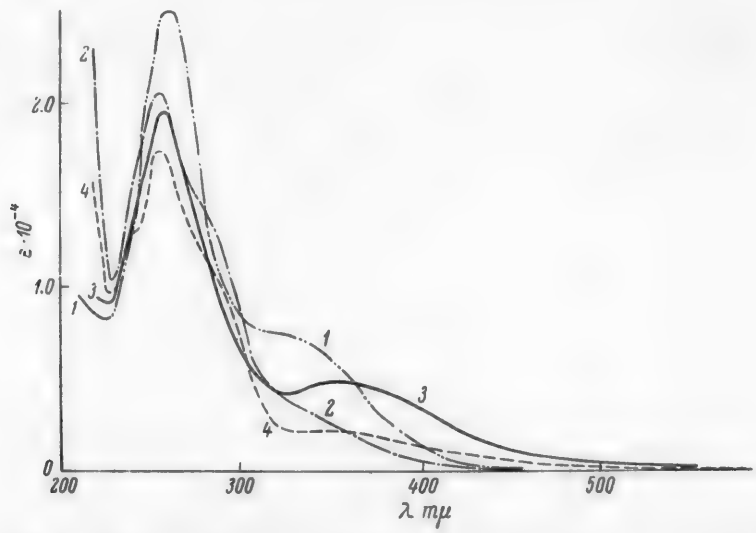
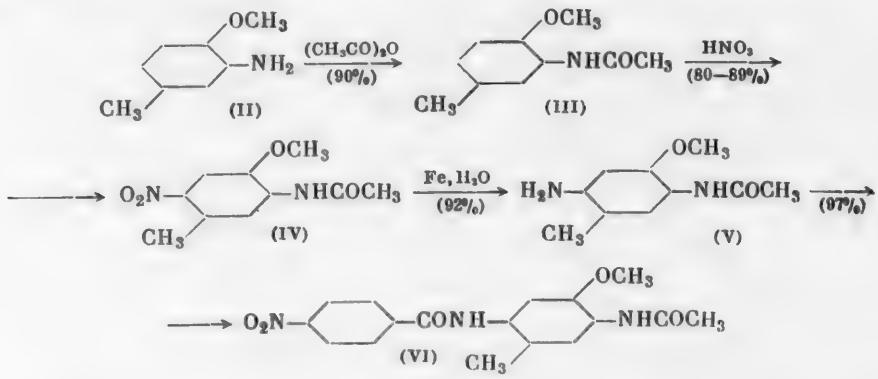


Fig. 3. Absorption spectra of 4'-nitrobenzanilide derivatives (I) in alcohol. The curve numbers correspond to the numbers of the compounds in Table 2. The curve designations are the same as in Fig. 1.

EXPERIMENTAL

No. 1. 4'-Nitro-4-acetamidobenzanilide [1-(4'-Nitrobenzamido)-4-acetamidobenzene] was prepared from N-acetyl-p-phenylenediamine and p-nitrobenzoyl chloride, dissolved in benzene containing a small amount of sodium carbonate. The compound was recrystallized 3 times from alcohol. Yellow crystals, m.p. > 300°.

No. 2. 4'-Nitro-5-methoxy-2-methyl-4-acetamidobenzanilide [1-(4'-Nitrobenzamido)-4-acetamido-5-methoxy-2-methylbenzene] (VI) is a new compound. It was synthesized as depicted in the following scheme (the optimum yields are given in parentheses).



a) 1-Acetamido-2-methoxy-5-methylbenzene (Acetylcresidine) (III). Cresidine (II) was sifted into acetic anhydride, taken in excess (10%). The mixture on cooling deposited crystals; recrystallization from a mixture of benzene and benzine (1:1) gave the compound as white needles, m.p. 113—114° [4] (according to [6], m.p. 110°).

The acetylation was also run by the technique [6, 7] of reacting acetic anhydride with cresidine in the presence of sodium acetate. A solution of cresidine in hydrochloric acid solution was treated with a 25% sodium acetate solution, and then the acetic anhydride was added with stirring. Silvery-white crystals deposited when the mixture was cooled. We obtained 16.5 g of acetylcresidine from 13.7 g of cresidine. After two recrystallizations from water, m.p. 112—113°.

b) 4-Nitro-1-acetamido-2-methoxy-5-methylbenzene (N-Acetyl-p-nitrocresidine) (IV) was prepared by the addition of nitric acid (d 1.48) to a solution of N-acetylcresidine in glacial acetic acid [8], by treatment with copper nitrate at 40—50° [9], and also by treatment with mixed acid at 0° [4]. The yield was only 67% when the mixed acid was composed of 3 parts of 12% sulfuric acid and 4 parts of 67% nitric acid. The mixed acid, containing the theoretical amount of nitric acid, was added in drops to a solution of 10 g of acetylcresidine in 30 ml of sulfuric acid at a temperature not exceeding 0°. Secondary processes were observed when either the temperature was raised or the amount of nitric acid was increased, leading to the formation of a sticky mass, which was completely soluble in alkali with an intense red color. This indicates that the use of a higher temperature leads not only to hydrolysis of the acetyl group, but also to the oxidation or hydrolytic cleavage of the methoxyl group. After adding all of the mixed acid, the stirring was continued for another 30—40 min and was stopped when the mass crystallized. The product was isolated by pouring over ice, filtered, washed with water, and recrystallized from alcohol, or even better, from aqueous alcohol. Yellow needles with m.p. 156°. The yield of pure product did not exceed 55%. By using a mixed acid of the proper composition and not allowing the nitration temperature to exceed 0° (external cooling), we were able to raise the yield to 89%, and even after only two recrystallizations the product had m.p. 156°.

For nitration we took 17.9 g (0.1 mole) of finely divided acetylcresidine and dissolved it with stirring in 30 ml of sulfuric acid (d 1.84) at a temperature not exceeding 0—5°. When all of the acetylcresidine had dissolved, the solution was cooled externally either with ice or dry ice to 0°, and then the mixed acid, prepared from nitric acid (d 1.5), was added at this temperature with stirring.

The hydrolysis of N-acetyl-p-nitrocresidine, m.p. 156°, with sodium hydroxide solution (heating on the boiling-water bath for 1—1.5 hr) gives 1-amino-4-nitro-5-methoxy-2-methylbenzene, obtained as yellow needles with m.p. 132°.

c) 1-Amino-4-acetamido-5-methoxy-2-methylbenzene (4-Amino-N-acetylcresidine) (V) [10]. Into a three-necked flask, fitted with a stirrer and reflux condenser, was charged 20 g of iron filings, 50 ml of water, and 0.5 ml of acetic acid. After heating (20 min) on the water bath, with stirring, the flask was cooled. A suspension of 22.4 g of finely divided nitroacetylcresidine in 100 ml of alcohol was added to the flask. The mixture was refluxed for 30 min, and then 2.5 g of iron filings was added. The mixture was heated until a yellow stain no longer appeared when the solution was tested with alcoholic caustic solution. After treating with a small amount of ammonium sulfide, the hot solution was filtered through a double filter. A small amount of hydrosulfite was added to the filtrate, and a part of the alcohol was distilled off. The residue on cooling deposited nearly colorless crystals. A single recrystallization from water containing 5% alcohol gave a product with m.p. 114.5° [10]. Yield 16.5 g (92%).

d) 4'-Nitro-5-methoxy-2-methyl-4-acetamidobenzanilide [1-(4'-Nitrobenzamido)-4-acetamido-5-methoxy-2-methylbenzene] (VI) is not described in the literature. To obtain this compound, we dissolved 19.4 g (0.1 mole) of p-amino-N-acetylcresidine in benzene and then added a water solution of sodium bicarbonate. This was followed by the addition of a solution of 19.4 g of p-nitrobenzoyl chloride in a small amount of benzene, with stirring. The precipitate was filtered and then recrystallized 3 times from alcohol. Yellow scale crystals, m.p. 251.5° (uncorrected).

Found %: N 12.12. $C_{17}H_{17}O_5N_3$. Calculated %: N 12.24.

No. 3. 4'-Nitro-4-aminobenzanilide (I, $A_1 = A_2 = H$, $A_3 = NH_2$). a) Preparation from 4'-nitro-4-acetamidobenzanilide. We were unable to hydrolyze the acetamido group in aqueous medium using either caustic solution or hydrochloric acid. The reaction fails to go under milder conditions, and the starting product was recovered. The use of more drastic conditions led to the formation of dark byproducts which indicated hydrolysis of the benzamido group with the formation of p-phenylenediamine. After examining the effect of the amount and concentration of hydrogen chloride in alcohol solution* and investigating the composition of the reaction products, we adopted the following procedure. A solution of 2.99 g (0.01 mole) of 4'-nitro-4-acetamidobenzanilide (see No. 1) in 100 ml of alcohol was prepared by heating the mixture in a flask fitted with a reflux condenser. Then 40 ml of 3 N hydrogen chloride solution in alcohol was added (with stirring, in small portions) to the solution in 30 min. The end of reaction is easily detected by the change in the color of the precipitate in the reaction flask: a precipitate of 4'-nitro-4-aminobenzanilide hydrochloride is formed, which we filtered and dissolved in water. Addition of ammonia to the water solution gave the free amine, which was filtered, washed, and then recrystallized 3 times from 50% alcohol. The compound was obtained as organge-red scale crystals with m.p. 226–227°, which agrees with the data in [11]. The compound is readily soluble in acetone and dichloroethane, moderately soluble in alcohol, and difficultly soluble in benzene and ether.

Found %: N 16.49. $C_{13}H_{11}O_3N_3$. Calculated %: N 16.34.

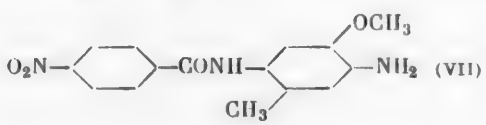
b) Preparation from 4'-nitro-4-formamidobenzanilide [11]. Hydrolysis of the formyl derivative is easily accomplished by heating 2 g of the compound with an aqueous solution of 2 N hydrochloric acid (500 ml).

4'-Nitro-4-formamidobenzanilide was recrystallized from methyl alcohol to give the compound as orange-yellow crystals with m.p. 238.5° (orange crystals were obtained when the compound was recrystallized from alcohol containing some pyridine). The hydrolysis product was obtained as golden-yellow scales.

Found %: N 16.28. $C_{13}H_{11}O_3N_3$. Calculated %: N 16.34.

If a smaller amount of acid is taken to hydrolyze the formyl derivative (100 ml for 1 g of compound), then the hydrochloride crystals have a slight yellow tinge.

No. 4. 4'-Nitro-5-methoxy-2-methyl-4-aminobenzanilide [1-(4'-Nitrobenzamido)-2-methyl-5-methoxybenzene (I, $A_1 = OCH_3$, $A_2 = CH_3$, $A_3 = NH_2$) (VII).



(VII)

*The alcoholic hydrogen chloride solution was prepared by saturating alcohol with gaseous hydrogen chloride which had been dried by passage through a Tishchenko flask containing sulfuric acid.

This compound is not reported in the literature. We obtained it by hydrolyzing the corresponding acetyl derivative (compound No. 2). We were able to accomplish this, using an alcoholic solution of hydrogen chloride, only after we had first studied the preparation of compound No. 3 from compound No. 1, since the use of either aqueous caustic or hydrochloric acid solution led to the formation of more profoundly changed products, or else the reaction failed to go. First we prepared a solution of 3.11 g (0.01 mole) of 4'-nitro-4-acetamido-5-methoxy-2-methylbenzanilide (compound No. 2) in 100 ml of methyl alcohol by heating the mixture under reflux on the water bath. Then 40 ml of a solution of hydrogen chloride in either methyl or ethyl alcohol (see No. 3) was added in 30 min. Heating the mixture for 2—3 hr yields a white precipitate of the hydrochloride. After distilling off a part of the alcohol, the precipitate was filtered, and then dissolved in water. The free amine was isolated by adding ammonia solution until the reaction was alkaline. The color of the precipitate ranges from orange-yellow to orange-red (depending on the concentration of the ammonia and the pH of the medium). Yield 2.69 g (89.7%). Two recrystallizations from alcohol gave the compound as bordeaux-colored crystals. M.p. 184.5°.

Found %: N 13.64. $C_{15}H_{15}O_4N_3$. Calculated %: N 13.95.

The absorption spectra of the powder surface were obtained as described in [2], based on measuring the reflection spectra of the solid compounds in powder form. They represent graphs of the reflection spectra (% R) in inverted form with the percent of light absorbed by the powder surface (% E) plotted along the ordinate. Such curves show more clearly the relative shifts in the absorption for the bathochromic and hypsochromic effects. The absorption spectra of the powder surface shown in Fig. 1 were obtained using a Beckman spectrophotometer, while those shown in Fig. 2 were obtained using a Hardy automatic spectrophotometer. The absorption spectra in solution were obtained using an SF-4 spectrophotometer.

The authors wish to thank B. A. Ikonnikov, S. F. Filippychev, and L. I. Belen'k for their cooperation in carrying out the present research.

SUMMARY

1. As had been shown earlier, a bathochromic shift of the spectral curves is observed when the two additional donors 2-OCH_3 (A_2) and 5-CH_3 (A_1) are introduced into compounds of structure (I), not containing groups A_3 = $NHCOCH_3$ or NH_2. In the present investigation it was shown that introducing the same groups in the same positions into compounds of the indicated structure, but containing groups A_3 = $NHCOCH_3$ or NH_2, no longer causes a bathochromic shift of the spectra. Instead a hypsochromic shift is observed, both for the absorption spectra of the powder surface and the absorption spectra in solution, especially in the long-wave portion of the spectral curves.

2. We postulate that these phenomena can be explained by the fact that introducing the CH_3 and OCH_3 groups disturbs the state of the electron shifts caused by the presence of peripheral NH_2 and $NHCOCH_3$ groups in the p-position. Further studies are needed to explain the mechanism of these shifts.

LITERATURE CITED

[1] V. A. Izmail'skii and A. V. Malygina, Zhur. Obshchei Khim. 29, 2623 (1959). *

[2] V. A. Izmail'skii and V. E. Limanov, Zhur. Obshchei Khim. 29, 2631, 2927 (1959). *

[3] A. V. Malygina, Dissertation: Absorption Spectra of Azo Dyes and p-Nitrobenzanilide Derivatives, Containing Several Electron-Donor Groups in One Ring [in Russian] (Moscow, 1955).

[4] V. I. Stavrovskaya, Dissertation: Investigations in the Domain of the Problem of the Auxochrome Groups. Nitrobenzoyl Derivatives of Arylamines. Concerning the Influence of the Methyl Group on Color in Polyauxochrome Systems [in Russian] (Moscow, 1936).

[5] V. A. Izmail'skii and A. M. Simonov, Zhur. Obshchei Khim. 16, 1670 (1946).

[6] L. Limpach, Ber. 22, 348, 790 (1889).

[7] N. N. Vorozhtsov, Principles of the Synthesis of Intermediate Products and Dyes [in Russian] (Goskhimizdat, Moscow, 1955), p. 535.

[8] N. N. Vorozhtsov and A. N. Titov, Zhur. Obshchei Khim. 6, 1298 (1936); 7, 357 (1937); Zhur. Priklad. Khim. 9, 1852 (1936); Soviet Author's Certificate No. 46,242.

*Original Russian pagination. See C. B. translation.

[9] H. E. Dadswell and J. Kenner, J. Chem. Soc. 585 (1927).

[10] German Patents 125,127 and 126,173.

[11] German Patent 206,968.

SYNTHESIS OF UNSATURATED METHYLENE AMIDES

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Translated from Zhurnal Obshchei Khimii. Vol. 29, No. 12, pp. 3943–3944, December 1959

Original article submitted December 4, 1958

The first unsaturated methyleneamides were synthesized by reacting acrylamide and its homologs with formaldehyde in the presence of acid catalysts [1]. Alkylidene(bis)acrylamides $(CH_2{=}CHCONH)_2CH(R)$ were obtained by the reaction of acrylonitrile with aldehydes in the presence of strong acids [2].

Methylene(bis)acryl- and methacrylamides were also obtained [3] when acryl- and methacrylamide were reacted with methylolmethacrylamide in the presence of hydrochloric acid as the catalyst. A study was also made of the reaction between acrylonitrile and N-methylolamides [4], leading to the formation of the acrylamide derivatives, $CH_2 = CHCONHCH_2NHCOR$.

N,N'-Methylene(bis)acrylamides are easily polymerized and can be copolymerized with other unsaturated compounds.

Information on the synthesis of methacrylamide derivatives of the mixed type is lacking in the literature. We synthesized several methacrylamide derivatives of this type by the condensation of methylolmethacrylamide with certain aromatic and aliphatic amides as indicated in the scheme below, using dichloroethane as the solvent and hydrochloric acid as the catalyst.

$$CH_2{=}C(CH_3)CONHCH_2OH + H_2NOCR \longrightarrow$$

$$\longrightarrow CH_2{=}C(CH_3)CONHCH_2NHCOR + H_2O + CH_2O$$

These same compounds can also be obtained by reacting methacrylamide with the appropriate methylolamides. The obtained unsaturated methylolamides are soluble in dichloroethane, acetone, alcohol, and certain other organic solvents.

EXPERIMENTAL

Starting Products. Methylolmethacrylamide (I) was obtained by reacting methacrylamide with paraformaldehyde in carbon tetrachloride medium [3]. The reaction was run in the presence of sodium ethylate [5]. After recrystallization from ethyl acetate, (I) had m.p. 54–55°.

Methylolacetamide (II) was obtained the same as indicated above by reacting acetamide with paraformaldehyde. After recrystallization from ethyl acetate, (II) had m.p. 51–52°.

N,N'-Methylenemethacrylacetyldiamide (III). A mixture of 3.44 g of methacrylamide and 3.56 g of (II) in 50 ml of dichloroethane, containing 0.5 ml of 36% hydrochloric acid, was heated with stirring at 60° for 5 hr. the reaction mixture, on cooling, depositedan amorphous solid, which was separated and dried to constant weight. Yield 4.9 g (77.5%). The crude product was purified by recrystallization from acetone, after which it had m.p. 155–155.5.

Found %: C 53.90; H 7.96; N 17.92. $C_7H_{12}O_2N_2$. Calculated %: C 53.81; H 7.73; N 17.95. Found %: Br 50.25. $C_7H_{12}O_2N_2Br_2$. Calculated %: Br 50.50.

N,N'-Methylenemethacrylisobutyryldiamide (IV). A mixture of 2.3 g of (I) and 1.74 g of isobutyramide in 20 ml of dichloroethane, containing 0.1 ml of 37% hydrochloric acid, was heated at 85° for 1 hour. Cooling of the mixture gave 2.8 g (76%) of (IV), which had m.p. 165–168° (after recrystallization from dichloroethane).

Found %: C 58.48; H 8.99; N 15.22. $C_9H_{16}O_2N_2$. Calculated %: C 58.69; H 8.75; N 15.22. Found %: Br 46.16. $C_9H_{16}O_2N_2Br_2$. Calculated %: Br 46.46.

N,N'-Methylenemethacrylbenzoyldiamide (V). A mixture of 2.3 g of (I), 2.4 g of benzamide, 20 ml of dichloroethane and 0.25 ml of hydrochloric acid (37%) was heated at 55° for 1 hour. We obtained 2.45 g (56%) of (V). After recrystallization from acetone, m.p. 148–149°.

Found %: C 66.00; H 6.64; N 12.23. $C_{12}H_{14}O_2N_2$. Calculated %: C 66.00; H 6.46; N 12.83. Found %: Br 42.28. $C_{12}H_{14}O_2N_2Br_2$. Calculated %: Br 42.28.

N,N'-Methylenemethacrylsalicyloyldiamide (VI). A mixture of 4.6 g of (I) and 5.48 g of salicylamide in 40 ml of dichloroethane, containing 0.22 ml of hydrochloric acid, was heated for 2 hr under reflux. We obtained 5.3 g of solid product (56.6%). After recrystallization from ethyl alcohol, m.p. 160–161°.

Found %: C 61.9; H 6.22; N 11.79. $C_{12}H_{14}O_2N_2$. Calculated %: C 61.49; H 6.02; N 11.96.

N,N'-Methylenemethacrylcrotonoyldiamide (VII). A mixture of 2.3 g of (I), 1.7 g of crotonamide, 20 ml of dichloroethane, and 0.55 ml of hydrochloric acid was heated with stirring at 70° for 1.5 hr. We obtained 3.16 g (86.8%) of (VII). After recrystallization from acetone, m.p. 159–160°.

Found %: C 59.01; H 7.75; N 15.32. $C_9H_{14}O_2N_2$. Calculated %: C 59.32; H 7.74; N 15.37. Found %: Br 63.45. $C_9H_{14}O_2N_2Br_4$. Calculated %: Br 63.69.

SUMMARY

Some unsaturated N,N'-methyleneamide compounds of the mixed type were synthesized by reacting amides with methylolamides.

LITERATURE CITED

[1] U. S. Patent 2,975,846 (1949).

[2] E. E. Magat, B. F. Faris, J. E. Reith, and L. F. Salisbury, J. Am. Chem. Soc. 73, 1028 (1951).

[3] H. Feuer and U. E. Lynch, J. Am. Chem. Soc. 75, 5027 (1953).

[4] E. E. Magat and L. F. Salisbury, J. Am. Chem. Soc. 73, 1035 (1951).

[5] I. A. Arbuzova, S. N. Ushakov, S. A. Plotkina, V. N. Efremova, and I. K. Ulezlo, Zhur. Obshchei Khim. 28, 1266 (1958). •

•Original Russian pagination. See C. B. translation.

ALKYLATION OVER ALUMINOSILICATE CATALYST ACTIVATED BY GASEOUS HYDROGEN CHLORIDE

III. ALKYLATION OF PHENOL WITH ISOBUTYL ALCOHOL

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Translated from Zhurnal Obshchei Khimii. Vol. 29, No. 12, pp. 3945–3947, December 1959

Originalarticle submitted October 22, 1958

In a previous paper one of us [1] had established that gumbrin, dried at 160–170° and treated with gaseous hydrogen chloride, shows a high catalytic activity. This new catalyst replaced aluminum chloride in the alkylation of benzene with alkyl halides. When used for the alkylation of phenol with isopropyl chloride, it proved to be more active than $AlCl_3$ [2]. It seemed of interest to investigate the behavior of gumbrin that had been treated with hydrogen chloride under theoretically different conditions, i.e., in reactions involving the cleavage of water. This would permit defining the mechanism of its action more precisely. For this reason, we decided to use gumbrin as a catalyst for the alkylation of phenol with a primary alcohol. It is known that the alkylation of phenols with primary alcohols goes with difficulty and requires a large amount of such catalysts as $AlCl_3$ and H_3PO_4 [3]. The vapor-phase alkylation of phenol over an aluminosilicate catalyst (gumbrin) at 320–500° appears to be a more promising technique. Such a technique was used in the alkylation of phenol with methyl and ethyl alcohols [4].

The difficulty with which primary alcohols alkylate phenol causes speculation that here other reactions, preceding direct alkylation of the ring, take place under the influence of the catalyst. These reactions can be: 1) isomerization of the primary alcohol to the tertiary alcohol [5] (tertiary alcohols readily alkylate phenol), and 2) dehydration of the primary alcohol with the formation of either the unsaturated hydrocarbon or of phenol ethers, with subsequent rearrangement of the latter to alkylphenols.

In this paper, we studied the alkylation of phenol with isobutyl alcohol in the presence of dry gumbrin, activated by gaseous hydrogen chloride at 120–150°. Here alkylphenol fractions (b.p. 190–241°) were obtained in a 14% yield, based on the phenol taken for reaction. The main reaction product proved to be p-tert-butylphenol. Some phenol ethers were formed at the same time, but only in trace amounts (0.5%). Dropping the reaction temperature to 114° failed to cause a substantial increase in the amount of ethers formed, but the yield of alkylphenols dropped sharply. Thise serves as evidence that, with the given molar ratio of alcohol to phenol (1:1), the formation of phenol ethers goes parallel with the alkylation of the ring, and is not the first stage of the reaction.

In order to ascertain the mechanism of the reaction we ran some additional experiments on the effect of gumbrin on isobutyl alcohol under the conditions of alkylating phenol. Here we established that unsaturated hydrocarbons are formed. It is possible that dehydration of the alcohol takes place first. The olefin formed here can either be activated by hydrogen chloride [6] or it can isomerize to the active tert-butyl chloride [7], and thus alkylate the benzene ring. This is supported by the fact that the alcohol radical suffers isomerization in alkylation. Only p-tert-butylphenol was isolated by us from the alkylphenol fractions. A smiliar isomerization was observed earlier by other investigators when phenol was alkylated with unsaturated hydrocarbons in the presence of BF_3 [8] or aluminum phenolate [6], and also when phenol was alkylated with alcohols in the presence of acid catalysts [3]. In contrast to the reaction using aluminum phenolate, in our case the p-isomer was formed, the same as is true of other acid catalysts. And despite the opinion expressed in the literature that the o-isomer is easily converted to the p-isomer in the presence of clays and acids [6], we were unable in our work to establish the formation of o-tert-butylphenol.

EXPERIMENTAL*

Into a three-necked flask, fitted with stirrer, reflux condenser, and bent inlet tube, was charged 50 g of gumbrin, previously dried at 160—170°, 74 g of phenol, and 15 g of isobutyl alcohol. The alcohol and phenol were first carefully dried and then distilled. A stream of hydrogen chloride was passed through the reaction mixture for an hour at 70—80°. After this the glass tube was replaced by a dropping funnel, and then with vigorous stirring, the remaining 46 g of isobutyl alcohol was added dropwise in 1 hour. The mixture was heated with constant stirring at 150° for 10 hr. The black pasty clay was allowed to settle, after which it was filtered and washed with ethyl ether. The filtrate was shaken once with water, and then repeatedly extracted with 10% caustic solution. Here two layers were formed. The upper layer contained phenol ethers, while the lower layer contained phenolates of the phenol and alkylphenols. The phenolates were decomposed with hydrochloric acid, and the liberated phenols and alkylphenols were extracted with ether, followed by drying of the ether solution over $MgSO_4$, and then distillation. After distilling off the ethyl ether and phenol, we obtained 17 g of alkylphenol fraction (b.p. 190—241°). This fraction was separated into four fractions by fractional distillation. Identification of the individual alkylphenols was accomplished by their conversion to the corresponding phenoxyacetic acids [9] and phenylurethans [10]. The phenylurethans were obtained by heating the alkylphenols in kerosene solution with phenyl isocyanate, while the phenoxyacetic acids were prepared by the method described in [11].

The 1st fraction, b.p. 190—200°, weighed 10.3 g, and had n_D^{20} 1.5428 and m.p. 46°. Recrystallization of this fraction from water gave prismatic crystals with m.p. 92°. After repeated recrystallization, the m.p. rose to 99°. The corresponding phenoxyacetic acid had m.p. 86°, while the phenylurethan melted at 147°. These constants correspond to p-tert-butylphenol; according to the literature, p-tert-butylphenol has m.p. 99°, the phenoxyacetic acid has m.p. 86.5° [9], and the phenylurethan has m.p. 147° [6]. The same fraction was also found to contain phenol, the phenoxyacetic acid derivative of which had m.p. 98°, while the phenylurethan had m.p. 124° [10].

The 2nd fraction, b.p. 200—212°, weighed 1.62 g, and had m.p. 50° and n_D^{20} 1.5390. Some crystals of tert-butylphenol were also isolated from this fraction. The fraction also contained a trace amount of phenol.

The 3rd fraction, b.p. 212-235°, weighed 1.5 g, and had m.p. 92°; 4th fraction, b.p. 235—241°, 3.33 g, m.p. 97°. The last two fractions after recrystallization had m.p. 99°, while their phenoxyacetic acid derivatives melted at 86°, and the phenylurethans melted at 147°. As a result, the main reaction product proved to be p-tert-butylphenol.

In order to isolate and identify the isomeric alkylphenols that could be present in the alkylphenol fractions, we took the latter and, after repeated recrystallization from alcohol, by chromatographing on aluminum oxide, separated them into a number of small fractions, which were then converted to the phenoxyacetic acids and the phenylurethans. However, we were unable to establish the presence of either isobutylphenols or o-tert-butylphenol. The layer containing the phenol ethers, was exceedingly small, and after drying and fractional distillation, we isolated from this layer 0.6 g of liquid with b.p. 216—233°, and n_D^{20} 1.5120. It is possible for this liquid to be phenol ethers. However, it was not studied in greater detail.

The alkylation of phenol with isobutyl alcohol also goes at 120°. Here the main product is again p-tert-butylphenol, but its yield drops to 12%; the amount of ethers formed is insignificant. The reaction hardly goes at 114°.

SUMMARY

Phenol was alkylated with isobutyl alcohol in the presence of gumbrin that had been activated with gaseous hydrogen chloride. The main reaction product proved to be p-tert-butylphenol.

LITERATURE CITED

[1] I. F. Radzevenchuk, Zhur. Obshchei Khim. 28, 2423 (1958).**

[2] I. F. Radzevenchuk, U. S. S. R. 116,610, Jan. 19, 1959; C. A. 53, 19970 h (1959).

*Student B. L. Smol'skii assisted in running the alkylation experiments.

**Original Russian pagination. See C. B. translation.

[3] Ad. Liebmann, Ber. 14, 1842 (1881); I. P. Tsukervanik and Z. N. Nazarova, Zhur. Obshchei Khim. 5, 767 (1935); 7, 623 (1937); Z. N. Nazarova and I. P. Tsukervanik, Zhur. Obshchei Khim. 10, 1151 (1940); N. G. Sidorova, Zhur. Obshchei Khim. 22, 962 (1952). •

[4] I. N. Samsonova, Zhur. Obshchei Khim. 27, 2697 (1957); • I. N. Samsonova and L. I. Khotyntseva, Zhur. Obshchei Khim. 27, 3189 (1957). •

[5] A. E. Chichibabin, Izvest. Akad. Nauk SSSR 951 (1935).

[6] R. Stroh, R. Seydel, and W. Hahn, Angew. Chem. 69, 699 (1957).

[7] V. I. Isagulyants and P. P. Bagryantseva, Neftyanoe Khoz. 2, 36 (1938).

[8] A. V. Topchiev, B. M. Tumerman, V. N. Andronov and L. I. Korshunova, Neftyanoe Khoz. 32, 7, 65 (1954).

[9] S. S. Nametkin, N. N. Mel'nikov, Yu. A. Baskakov and K. S. Bokarev, Zhur. Anal. Khim. 5, 7 (1950).

[10] W. Steinkopf and T. Höpner, J. prakt. Chem. 113, 141 (1926).

[11] C. F. Koelsch, J. Am. Chem. Soc. 53, 304 (1931).

•Original Russian pagination. See C. B. translation.

SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

XIII. SYNTHESIS AND INVESTIGATION OF THE STRUCTURE OF DERIVATIVES OF DICHLOROETHANE- AND DICHLOROPROPANEPHOSPHONIC ACIDS

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Translated from Zhurnal Obshchei Khimii. Vol. 29, No. 12 pp. 3947-3953, December 1959

Original article submitted November 20, 1958

The oxidative chlorophosphonation of paraffins and chloroparaffins using phosphorus trichloride can yield the isomeric chlorides of the corresponding alkane- and chloroalkanephosphonic acids [1]. Olefins are also capable of yielding isomers in this reaction. The structure of these isomers is determined by the manner in which the chlorine atom and the $POCl_2$ moiety add to the double bond. For example, in the case of propylene, the two isomers formed have the structure $CH_3CHClCH_2P(O)Cl_2$ and $CH_3CH(CH_2Cl)P(O)Cl_2$ [2].

It seemed probably to us that investigating the reaction of phosphorus trichloride with halo-substituted olefins and oxygen would make it possible to establish the formation of the isomeric dichlorides more clearly than in the case of the unsubstituted ethylenic hydrocarbons.

With this in mind, a study of the oxidative chlorophosphonation of vinyl chloride and allyl chloride was made in the present paper.

It proved that vinyl chloride reacts with phosphorus trichloride and oxygen to yield the mixed isomeric dichlorides of dichloroethanephosphonic acid: $CH_2ClCHClP(O)Cl_2$ and $CHCl_2CH_2P(O)Cl_2$. The reaction with vinyl chloride was run both at low temperatures (-40°), by passing oxygen into a mixture of liquid vinyl chloride and phosphorus trichloride, and at higher temperatures (up to +20°), by adding a mixture of gaseous vinyl chloride and oxygen to phosphorus trichloride. Identical results were obtained in both cases. The yields of mixed isomeric dichloroethanephosphonic dichlorides (nearly 70%, based on reacted vinyl chloride) proved to be considerably greater than those observed in the oxidative chlorophosphonation of either ethane or ethylene. The obtained mixture of chlorides distilled in a narrow temperature range (70—73° at 2 mm), which made it impossible to show that it contained isomers or to effect the separation of the latter into the pure components by simple fractional distillation.

The formation of the isomers was shown by subjecting the isolated mixture of dichlorides to a series of consecutive transformations. When reacted with an excess of various alcohols at comparatively low temperatures (0—5°), the starting mixture of chlorides was converted to a mixture of the corresponding dichloroethanephosphonic esters, which, however, also distilled in a narrow temperature range. Treatment of the mixture of isomeric dichloroethanephosphonic esters with triethylamine led to the cleavage of hydrogen chloride and the separation of triethylamine hydrochloride. However, the cleaved amount of hydrogen chloride was only 30—35%. • The use of a larger excess of triethylamine and raising the temperature of the reaction mass to 60—70° failed to alter the dehydrochlorination results. As a result, after reaction with triethylamine and removal of the hydrochloride precipitate of the latter, the reaction mixture proved to contain two compounds that differed sharply in their boiling points, which

•Based on the assumption that it is possible to cleave only one mole of hydrogen chloride under these conditions.

made it possible to isolate two pure compounds in each case.

In the case of the dibutyl ester of dichloroethanephosphonic acid, we were able to show that the unreacted dibutyl ester is the derivative of 1,2-dichloroethanephosphonic acid. Its structure was shown by dehalogenation with zinc dust, and here the dibutyl ester of ethenephosphonic acid (XX) was formed. The structure of the latter was shown by elemental analysis, the absence of chlorine in the compound, its avid absorption of bromine, the molecular weight and molecular refraction values, and the presence of the frequencies characteristic for the C=C bond in the infrared absorption spectrum of the compound.

The formation of (XX) under the described conditions could have occurred only by the dehalogenation of a compound having two chlorine atoms on adjacent carbon atoms. Only the dibutyl ester of 1,2-dichloroethanephosphonic acid (XI) could have been such a compound. The obtained results clearly show that the second isomer, contained in the starting mixture of esters (prior to treatment with triethylamine), was the dibutyl ester of 2,2-dichloroethanephosphonic acid.

The discussed observations testify to the validity of the theory expressed above that in the oxidative chlorophosphonation of vinyl chloride, the addition of the chlorine atom and the $POCl_2$ radical goes in two directions. The following scheme shows the described course of the transformations.

$$CH_2{=}CHCl \xrightarrow[-POCl_3]{PCl_3 + O_2} \begin{cases} CH_2ClCHClP(O)Cl_2 \\ CHCl_2CH_2P(O)Cl_2 \end{cases} \xrightarrow{ROH} \longrightarrow$$

$$\longrightarrow \begin{matrix} CH_2ClCHClP(O)(OR)_2 \\ CHCl_2CH_2P(O)(OR)_2 \end{matrix} \Big\} \xrightarrow{(C_2H_5)_3N} \begin{matrix} CH_2ClCHClP(O)(OR)_2 \\ CHCl{=}CHP(O)(OR)_2 \end{matrix} \xrightarrow[ROH]{Zn} CH_2{=}CHP(O)(OR)_2$$

The above described technique of preparing esters of dichloroethanephosphonic acid by reacting the chlorides of the latter with a large excess of an alcohol proved to be inapplicable to secondary alcohols (isopropyl, sec-butyl). In these cases, the formation of sirupy liquids occurred, which decomposed on distillation with the formation of olefins. We found that the esters of secondary alcohols could be obtained by reacting dichloroethanephosphonic chloride with the proper alcohols in the presence of triethylamine. Here two esters were formed—the ester of 2-chloroethenephosphonic acid and the ester of 1,2-dichloroethanephosphonic acid, which could be separated into the pure compounds by fractional distillation.

The following observation also indicates that two isomeric chlorides are formed in the oxidative chlorophosphonation of vinyl chloride. A mixture of the isomeric dichloroethanephosphonic chlorides was passed in vapor form through a heated glass tube, filled with activated carbon, which, as is known, facilitates thermal dehydrochlorination [3]. Together with dehydrochlorination, which resulted in the formation of 2-chloroethenephosphonic dichloride (III), in the discussed case there were also more profound transformations: we were able to isolate phosphorus oxychloride and 1,2-dichloroethylene from the reaction products. The fact that the latter is obtained is evidence that 1,2-dichloroethanephosphonic dichloride (II) is formed in the oxidative chlorophosphonation of vinyl chloride. In its physical constants, (II) corresponded to the chloride that we had obtained earlier from acetylene, phosphorus trichloride, and oxygen [4].

The chlorides obtained by the two indicated methods were subjected to hydrolysis. The isolated phosphonic acids were converted to their aniline salts, which failed to give a mixed melting point depression (192–193°).

Allyl chloride was the second chloroolefin that we used in the investigated reaction. The oxidative chlorophosphonation of this compound gave dichloropropanephosphonic dichloride (IV) in about 80% yield. Also in this case it could be expected that the reaction goes in two directions.

$$CH_2{=}CHCH_2Cl + PCl_3 + O_2 \longrightarrow \begin{cases} \longrightarrow CH_2ClCHClCH_2P(O)Cl_2 \\ \longrightarrow (ClCH_2)_2CHP(O)Cl_2 \end{cases}$$

To establish the direction of reaction, the obtained chloride (IV) was converted to the diethyl ester of dichloropropanephosphonic acid (XIV), which was then subjected to dehalogenation using zinc dust in methanol. Here, depending on the structure of the starting chloride, it is possible for two diethyl esters to arise, having the structures corresponding to the formulas:

$CH_2=CHCH_2P(O)(OC_2H_5)_2$ and

We were able to isolate one of these compounds (XXI). Evidence in support of this is the fact that the constants of the isolated compound coincide with the constants of the ester obtained by the Arbuzov method, and also with the literature data [5]. In addition, a study of the infrared spectrum of this compound revealed the presence of the frequencies characteristic for the C=C bond and failed to show the presence of lines inherent to the three-membered ring. As a result, it was shown that the compound CH_2 ClCHClCH$_2$ P(O)Cl$_2$ is formed in the oxidative chlorophosphonation of allyl chloride. However, the low yield obtained does not permit excluding the formation of a second isomeric chloride. The constants of the compounds obtained by us are given in the table.

TABLE

Compound	Formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Yield (in %)
I	$C_2H_3Cl_2P(O)Cl_2$ *	74—75° (2.5) 208—210 (750)	1.6376	1.4998	38.79	39.92	66
II	$CH_2ClCHClP(O)Cl_2$ **	83—86 (5)	1.6399	—	—	39.22	59
III	$CHCl=CHP(O)Cl_2$	184—186 (750)					
IV	$CH_2ClC_2H_3ClP(O)Cl_2$	104—107 (3)	1.5891	1.5073	43.4	43.8	79
V	$CH_2ClC_2H_3ClP(O)(OH)_2$	m.p. 67—68°	—	—	—	—	—
VI	$C_2H_3Cl_2P(O)(OC_2H_5)_2$ *	108—111 (3)	1.2800	1.4487	49.2	50.51	88
VII	$CH_2ClCHClP(O)(OC_2H_5)_2$	110—111 (3)	1.2810	1.4496	49.2	50.51	—
VIII	$C_2H_3Cl_2P(O)(OC_3H_7)_2$ *	127 (2)	1.2066	1.4463	59.04	59.74	66
IX	$CH_2ClCHClP(O)[OCH(CH_3)_2]_2$	115—118 (3)	1.1877	1.4395	58.4	59.74	—
X	$C_2H_3Cl_2P(O)(OC_4H_9)_2$ *	134—136 (3)	1.1583	1.4510	67.34	68.98	74
XI	$CH_2ClCHClP(O)(OC_4H_9)_2$	143—145 (3)	1.1548	1.4492	67.62	68.98	—
XII	$C_2H_3Cl_2P(O)[OCH(CH_3)(C_2H_5)]_2$ *	70 (1.10^{-4})	1.1305	1.4500	69.14	68.98	—
XIII	$CH_2ClC_2H_3ClP(O)(OCH_3)_2$	111 (3)	1.3537	1.4685	45.35	45.89	75
XIV	$CH_2ClC_2H_3ClP(O)(OC_2H_5)_2$	116—118 (3)	1.2457	1.4570	54.45	55.18	89
XV	$CH_2ClC_2H_3ClP(O)(OCH_2CH=CH_2)_2$	137—140 (2)	1.2310	1.4799	62.98	62.91	7
XVI	$CHCl=CHP(O)(OCH_3)_2$	76—78 (4)	1.2816	1.4445	35.93	35.70	36
XVII	$CHCl=CHP(O)(OC_2H_5)_2$	80—81 (3)	1.1608	1.4436	45.31	45.17	—
XVIII	$CHCl=CHP(O)[OCH(CH_3)_2]_2$	90—93 (3)	1.0979	1.4395	54.32	54.41	—
XIX	$CHCl=CHP(O)(OC_4H_9)_2$	119—120 (4)	1.0712	1.4502	63.89	63.65	—
XX	$CH_2=CHP(O)(OC_4H_9)_2$	101—102 (1.5)	0.9757	1.4300	58.23	58.78	—
XXI	$CH_2=CHCH_2P(O)(OC_2H_5)_2$ ***	90—91 (12)	1.0380	1.4312	44.41	44.4	—

*Mixture of isomers.

**The compound obtained by the oxidative chlorophosphonation of 1,2-dichloroethane had b.p. 70-72° (2 mm) and d_4^{20} 1.6371 [1].

***The diethyl allylphosphonate obtained by the Arbuzov method had b.p. 91—93° (12 mm), d_4^{20} 1.0378, n_D^{20} 1.4320.

EXPERIMENTAL

1. Dichloroethanephosphonic dichlorides (I). a) Oxygen was passed through a mixture of 600 g of phosphorus trichloride and 100 g of vinyl chloride at -40 to -30° until reaction ceased. We recovered 38.7 g of vinyl chloride from the reaction mass. We also isolated 140.6 g of (I).

Found %: C 11.16, 11.50; H 1.95, 2.30; P 14.53; Cl 65.52. M 217.6. $C_2H_3OPCl_4$. Calculated %: C 11.11; H 1.40; P 14.35; Cl 65.73. M 215.86.

b) Analogous results were obtained when a mixture of equal volumes of vinyl chloride and oxygen was passed into phosphorus trichloride at 20—25°.

2. Dehydrochlorination of dichloroethanephosphonic dichloride. Sixty grams of (I) in a distillation flask was heated to the boil at 20 mm. The vapors from the flask passed in succession through: a glass tube (d 12 mm), heated

in a furnace at 180° and filled with 15 g of dry activated carbon; a receiver; and a wash bottle filled with caustic solution. The amount of product in the receiver was 38.1 g, and the amount of hydrogen chloride abosrbed by the caustic solution was 8.4 g. Fractionation of the distillate in vacuo (3–5 mm) gave: 1) condensate from the trap cooled to -70°, 18.2 g; 2) liquid with b.p. up to 78°; and 3) residue 1.6 g.

From the condensate we isolated at atmospheric pressure:

a) a substance that after washing with water and drying over sodium sulfate had b.p. 61–62°, d_4^{20} 1.2882, n_D^{20} 1.4480, MR_D 20.13, M 95.3. According to the literature, cis-1,2-dichloroethylene has b.p. 60°, d_4^{15} 1.2913, n_D^{15} 1.4519, MR_D 20.70, M 96.96;

b) a fraction with b.p. 105–108°, and d_4^{20} 1.6527.

Found %: Cl 69.4, 69.9; $OPCl_3$. Calculated %: Cl 69.2.

From the fraction distilling up to 78° (3–5 mm), we isolated (III) at atmospheric pressure.

Found %: C 13.40, 13.17; H 1.40, 1.60; P 17.32, 17.21. M 182.3. $C_2H_2OPCl_3$. Calculated %: C 13.38; H 1.11; P 17.27. M 179.5.

$ClCH{=}CHP(O)Cl_2$, obtained by the oxidative chlorophosphonation of acetylene, had b.p. 184–186° [4].

Hydrolysis of (III) gave the corresponding acid, the aniline salt of which failed to depress the melting point when mixed with the aniline salt obtained from the earlier synthesized 2-chloroethenephosphonic acid.

3. Dichloropropanephosphonic dichloride (IV). Oxygen was passed at 0–10° through a mixture of 50.0 g (0.65 mole) of allyl chloride and 250 g (1.8 moles) of phosphorus trichloride until reaction ceased. We recovered 23 g of allyl chloride from the reaction. We also obtained 64.2 g of (IV).

Found %: C 15.75, 15.90; H 2.07, 2.09; P 13.35, 13.72; Cl (hydrolyzable) 30.67, 31.04; Cl (total amount) 61.45. M 234.2. $C_3H_5OPCl_4$. Calculated %: C 15.65; H 2.17; P 13.47; Cl (hydrolyzable) 30.87; Cl (total amount) 61.74. M 229.89.

Dichloropropanephosphonic acid (V). Hydrolysis was accomplished by treating 10.5 g of (IV) with 39 ml of water. The excess water and hydrogen chloride were removed in vacuo. The residue was dried at 90° (3 mm). White crystals with m.p. 67–68° were obtained.

Found %: C 18.11, 18.29; H 3.89; 3.57; H (act.) * 1.06, 1.03. $C_3H_7O_3PCl_2$. Calculated %: C 18.65; H 3.62; H (act.) 1.04.

4. Diethyl esters of isomeric dichloroethanephosphonic acids (VI). We added 21.6 g (0.1 mole) of (I) dropwise to 46.0 g (1.0 mole) of anhydrous ethyl alcohol at -5°. We isolated 20.75 g of (VI).

Found %: C 30.56, 30.45; H 5.75, 5.71; P 12.95, 13.12; Cl 29.82, 30.23. M 233.4. $C_6H_{13}O_3PCl_2$. Calculated %: C 30.65; H 5.53; P 13.20; Cl 30.17. M 235.06.

5. Diethyl esters of 2-chloroethenephosphonic acid (XVII) and 1,2-dichloroethanephosphonic acid (VII). We added 47.0 g (0.2 mole) of (VI) to a solution of 20.2 g (0.2 mole) of triethylamine in 80 ml of dry ether. The next day, the triethylamine hydrochloride was filtered and washed with ether. We obtained 8.6 g (31.2%) of the salt. From the ether solution, we isolated by fractionation, 10.0 g of low-boiling compound (XVII):

Found %: C 36.19, 36.54; H 6.46, 6.30, P 16.16, 16.73; Cl 17.53. M 204.7. $C_6H_{12}O_3PCl$. Calculated %: C 36.27; H 6.04; P 15.82; Cl 17.88. M 198.59.,

and 20.0 g of high-boiling compound (VII).

Found %: P 12.87, 12.72. M 238.5. $C_6H_{13}O_3PCl_2$. Calculated %: P 13.20. M 235.06.

6. Dipropyl esters of isomeric dichloroethanephosphonic acids (VIII). From 10.0 g (0.046 mole) of (I) and 50 ml of n-propanol, under the conditions of Expt. 4, we obtained 8.0 g of (VIII).

*The amount of "active" hydrogen was determined using the data in [6].

Found %: C 36.31, 36.49; H 7.06, 7.17; P 11.61. $C_8H_{17}O_3PCl_2$. Calculated %: C 36.51; H 6.51; P 11.77.

7. Disopropyl esters of 1,2-dichloroethanephosphonic acid (IX) and 2-chloroethenephosphonic acid (XVII).

a) Using the conditions of Expt. 4, we were unable to isolate the mixed diisopropyl esters of the isomeric dichloroethanephosphonic acids, due to complete conversion to tar in the distillation.

b) We added 43.2 g (0.2 mole) of (I) in drops to a mixture of 42.0 g (0.7 mole) of isopropyl alcohol and 60.6 g (0.6 mole) of triethylamine at -5°. The triethylamine hydrochloride precipitate was filtered. From the filtrate we isolated two fractions, having the boiling points: 1) 80–97° (3 mm), 8.2 g, and 2) 100–120° (3 mm), 17.6 g.

Compound (IX) was isolated from the 100–120° fraction.

Found %: C 36.41, 36.59; H 7.2, 6.88; P 11.66, 11.71. $C_8H_{17}O_3PCl_2$. Calculated %: C 36.51; H 6.51; P 11.77.

We isolated 5.2 g of (XVIII) when the 80–97° (3 mm) fraction was redistilled.

Found %: C 42.24, 42.48; H 7.22, 7.46; P 13.42, 13.56. $C_8H_{16}O_3PCl$. Calculated %: C 42.38; H 7.06; P 13.68.

8. Dibutyl esters of isomeric dichloroethanephosphonic acids (X). Using the conditions of Expt. 4, we isolated 21.5 g of (X) from 21.6 g (0.1 mole) of (I) and 59.0 g (0.8 mole) of n-butanol.

Found %: C 41.30, 41.54; H 8.30, 7.97; P 11.40, 11.23; Cl 25.20, 25.20. M 296.5. $C_{10}H_{21}O_3PCl_2$. Calculated %: C 41.21; H 7.21; P 10.65; Cl 24.40. M 291.17.

9. Dibutyl esters of 2-chloroethenephosphonic acid (XIX) and 1,2-dichloroethanephosphonic acid (XI). Using the conditions of Expt. 5, we obtained 6.0 g of (XIX) from 29.1 g (0.1 mole) of (X).

Found %: C 47.29, 47.42; H 8.42, 8.22; P 12.64, 12.21. M 258.5. $C_{10}H_{20}O_3PCl$. Calculated %: C 47.15; H 7.85; P 12.16. M 254.7.

We also isolated 14.2 g of unreacted (X).

Found %: C 40.38, 40.15; H 7.30, 7.63; P 10.83, 10.70. M 287. $C_{10}H_{21}O_3PCl_2$. Calculated %: C 41.21; H 7.21; P 10.65. M 291.17.

10. Sec-butyl esters of isomeric dichloroethanephosphonic acids (XII). A solution of 21.6 g (0.1 mole) of (I) in 100 ml of ether was added at -20° to a mixture of 15.0 g (0.2 mole) of sec-butyl alcohol and 20.2 g (0.2 mole) of triethylamine in 100 ml of ether. After removal of the triethylamine hydrochloride and solvent we obtained 20.0 g of light-brown liquid (~ 70%). We isolated a small amount of impure (XII) when the liquid was distilled in a high vacuum.

Found %: C 39.58, 39.61; H 7.14, 7.33; OC_4H_9 47.02. $C_{10}H_{21}O_3PCl_2$. Calculated %: C 41.24; H 7.27; OC_4H_9 50.21.

The distillation trap, cooled in liquid air, contained 3.5 g of a substance that completely reacted with Br_2.

B.p. 157°, d_4^{20} 1.7807, n_D^{20} 1.5115.
2,3-Dibromobutane has b.p. 157–158°, d_4^{20} 1.7831, n_D^{20} 1.5147 [7].

11. Dimethyl ester of dichloropropanephosphonic acid (XIII). Using the conditions of Expt. 4, we obtained 16.5 g of (XIII) from 23.0 g (0.1 mole) of (IV).

Found %: P 13.91, 13.89; Cl 32.56, 32.29. M 227.0. $C_5H_{11}O_3PCl_2$. Calculated %: P 14.02; Cl 32.12. M 221.03.

12. Diethyl esterof dichloropropanephosphonic acid (XIV). Using the conditions of Expt. 4, we obtained 36.0 g of (XIV) from 34.5 g (0.15 mole) of (IV).

Found %: C 33.84, 33.94; H 7.06, 7.03. M 243.0. $C_7H_{15}O_3PCl_2$. Calculated %: C 33.73; H 6.02. M 249.1.

13. Diallyl ester of dichloropropanephosphonic acid (XV). Using the conditions of Expt. 4, we obtained 4.1 g of (XV) from 46.0 g (0.2 mole) of (IV).

Found %: C 39.60, 39.72; H 5.16, 5.10; P 11.03, 11.06; Cl 25.89, 25.59. M 270.3. $C_9H_{11}O_3PCl_2$. Calculated %: C 39.55; H 5.49; P 11.35; Cl 26.00. M 273.1.

14. Dimethyl ester of 2-chloroethenephosphonic acid (XVI). Using the conditions of Expt. 5, we obtained 20.0 g of (XVI) from 52.0 g (0.25 mole) of the dimethyl ester of dichloroethanephosphonic acid (mixture of isomers [8]).

Found %: OCH_3 37.13, 36.87. $C_4H_8O_3PCl$. Calculated %: OCH_3 36.38.

15. Dibutyl ester of ethenephosphonic acid (XX). We added 10.6 g (0.036 mole) of (X) to a mixture of 18.5 g of zinc dust (activated with copper sulfate) and 60 ml of butanol. The reaction mass was heated on the boiling water bath for 4 hr, and the compound was isolated by fractional distillation.

Found %: C 54.36, 54.42; H 9.82, 10.01; P 13.92, 14.01. M 223.45. $C_{10}H_{22}O_3P$. Calculated %: C 54.54; H 9.54; P 14.09. M 220.25.

16. Diethyl ester of allylphosphonic acid (XXI). With vigorous stirring, 37.0 g (0.15 mole) of (XIV) was added in drops to a mixture of 52 g of zinc dust and 120 ml of methanol. The reaction mass was heated under reflux for 2 hours. We isolated 4.5 g of (XXI).

Found %: C 47.49, 47.50; H 8.64, 8.90; P 17.13, 16.97. $C_7H_{15}O_3P$. Calculated %: C 47.19; H 8.42; P 17.22.

17. 1,2-Dichloroethanephosphonic dichloride (II). A charge of 35.0 g (0.15 mole) of (VII) and 62.0 g (0.3 mole) of phosphorus pentachloride was placed in a distilling flask fitted with a column. The mixture was heated for 2 hr at 90–110°, after which 19.2 g of (II) was distilled from the residue.

SUMMARY

1. The oxidative chlorophosphonation of both vinyl chloride and allyl chloride was accomplished.

2. It was shown that the oxidative chlorophosphonation of vinyl chloride yields two isomeric chlorides, corresponding to 2,2- and 1,2-dichloroethanephosphonic acid.

3. A number of esters of dichloroethane-, 2-chloroethene-, and dichloropropanephosphonic acid were synthesized.

LITERATURE CITED

[1] L. Z. Soborovskii, Yu. M. Zinov'ev and M. A. Énglin, Doklady Akad. Nauk SSSR 73, 333 (1950).

[2] L. Z. Soborovskii, Yu. M. Zinov'ev and L. I. Muler, Doklady Akad. Nauk SSSR 109, 98 (1956). •

[3] Austrian Patent 179,289 (1954); Chem. Zentr. 1837 (1955); Yu. M. Zinov'ev and L. Z. Soborovskii, Zhur. Obshchei Khim. 29, 615 (1959). •

[4] Yu. M. Zinov'ev, L. I. Muler and L. Z. Soborovskii, Zhur. Obshchei Khim. 24, 380 (1954). •

[5] L. N. Parfent'ev, Uchenye Zapiski Kazan. Univ. 1, 52 (1928); M. Kh. Shafiev, Trudy Samarkand. Uchitel. Instit. 5, 29 (1947); A. E. Arbuzov and A. I. Razumov, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk 714 (1951).

[6] A. P. Terent'ev and A. I. Kireeva, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk 172 (1951).

[7] Handbook of Chemistry [in Russian] (State Chemical and Technical Press, 1951). Vol. 2.

[8] Yu. M. Zinov'ev, V. N. Kulakova and L. Z. Soborovskii, Zhur. Obshchei Khim. 28, 1551 (1958). •

•Original Russian pagination. See C. B. translation.

FULL ESTERS OF SOME HALOGENATED ALKANE- AND ALKENEPHOSPHONIC ACIDS

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Translated from Zhurnal Obshchei Khimii. Vol. 29, No. 12, pp. 3954–3956, December 1959

Original article submitted November 20, 1958

Earlier we had shown that the oxidative chlorophosphonation of haloalkanes, olefins, and mono- and dihaloolefins leads to the formation of the chlorides of mono-, di-, and trihaloalkanephosphonic acids [1, 2]. The alkyl esters of such acids have hardly been studied. At the same time, because they are quite readily available, the indicated compounds deserve consideration as possible insecticides and as starting materials for the preparation of esters of unsaturated phosphonic acids, which might find utility as monomers in the synthesis of phosphorus-containing and related polymers.

In this paper we prepared a number of full esters of some halogenated alkane- and alkenephosphonic acids (see table), which were synthesized by utilizing the chlorides, in turn obtained by the oxidative chlorophosphonation of the corresponding hydrocarbons or halo derivatives of the latter.

The methyl and ethyl esters of chloropropanephosphonic acid were synthesized from the acid chloride of the latter (obtained by the oxidative chlorophosphonation of propylene), as well as from compounds that were not a mixture of isomers and had a rigidly established structure. For this reason, a difference in the values of the physical constants for compounds (I) and (II), and also for (III), (IV) and (V), can be regarded as proof that compounds (I) and (III) contain the isomeric esters of 2-chloro-1-propanephosphonic and 1-chloro-2-propanephosphonic acids.

EXPERIMENTAL

1. Dimethyl esters of chloropropanephosphonic acid (I) and (II). a) For the esterification we took 40.6 g (0.21 mole) of chloropropanephosphonic dichloride, obtained by the oxidative chlorophosphonation of propylene [3], and added it at -5° to 200 ml of methanol. We isolated 29.65 g of (I).

Found %: C 32.80, 33.10; H 6.06, 5.66; Cl 19.16; OCH_3 32.88, 32.54. $C_5H_{12}O_3PCl$. Calculated %: C 32.18; H 6.48; Cl 19.00; OCH_3 32.26.

b) Using 8.83 g of the dichloride, synthesized by the method of Bergmann and Bondi [4] from propylene and phosphorus pentachloride, and the same conditions as in (a), we obtained 6.8 g of (II).

Found %: OCH_3 32.68, 32.24. $C_5H_{12}O_3PCl$. Calculated %: OCH_3 33.26.

2. Diethyl esters of chloropropanephosphonic acid (mixture of isomers, III), 2-chloro-1-propanephosphonic acid (IV) and 1-chloro-2-propanephosphonic acid (V). Using conditions of Expt. 1. a) From 74.0 g of chloropropanephosphonic dichloride, obtained in the oxidative chlorophosphonation of propylene, we obtained 64 g of (III).

Found %: Cl 16.18, 16.38. M 214.94. $C_7H_{16}O_3PCl$. Calculated %: Cl 16.52. M 214.64.

b) From 8.0 g of 2-chloro-1-propanephosphonic dichloride, obtained in the oxidative chlorophosphonation of 2-chloropropane, we obtained 4.5 g of (IV).

Found %: Cl 16.75, 15.90; OC_2H_5 42.88. $C_7H_{16}O_3PCl$. Calculated %: Cl 16.52; OC_2H_5 41.98.

TABLE

Compound	Formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Yield, %
I	$C_3H_6ClP(O)(OCH_3)_2$ *	93—96° (5)	1.2213	1.4470	40.81	41.02	76
II	$CH_3CHClCH_2P(O)(OCH_3)_2$	100—102 (6)	1.2144	1.4465	41.74	41.02	87
III	$C_3H_6ClP(O)(OC_2H_5)_2$ *	115—118 (6)	1.1222	1.4396	50.26	50.02	79
IV	$CH_3CHClCH_2P(O)(OC_2H_5)_2$	105—107 (6)	1.1285	1.4370	49.84	50.02	51
V	$CH_3CH(CH_2Cl)P(O)(OC_2H_5)_2$	126—128 (10)	1.1295	1.4395	49.87	50.02	67
VI	$C_3H_6FP(O)(OC_2H_5)_2$ *	57 (2)	1.0433	1.4193	47.16 **	45.36	36
VII	$CHCl_2CHClP(O)(OC_2H_5)_2$	134—135 (4)	1.3559	1.4530	53.28 **	54.69	80
VIII	$CHCl_2CHClP(O)(OC_3H_7)_2$	145—148 (3)	1.2888	1.4512	62.25 **	64.61	89
IX	$C_2H_2FCl_2P(O)(OC_2H_5)_2$ *	121—122 (5)	1.3384	1.4286	48.0 **	50.48	93
X	$CHFClCHClP(O)(OC_2H_5)_2$	103—106 (3)	1.3349	1.4230	48.4 **	50.48	—
XI	$C_2H_2FCl_2P(O)(OC_3H_7)_2$	120 (2)	1.2684	1.4328	57.8	59.81	38
XII	$CH_2ClCH_2CH(CH_3)P(O)(OC_4H_9)_2$	148—153 (3)	1.0464	1.4470	72.26 **	73.35	73
XIII	$C_2H_3ClBrP(O)(OC_2H_5)_2$ *	130 (2)	1.4927	1.4752	52.12	53.41	47
XIV	$CHCl{=}CClP(O)(OC_2H_5)_2$	108 (7)	1.3163	1.4460	47.4 **	50.04	33
XV	$CHF{=}CClP(O)(OC_2H_5)_2$	80—82 (3)	1.2487	1.4090	38.86 **	40.28	27

*Mixture of isomers.

**For the di- and trihaloalkanephosphonic acid derivatives, the value of the molecular refraction is quite different from the calculated value, despite the satisfactory analysis results. The reason for such deviation has not been established yet.

c) From 13.1 g of 1-chloro-2-propanephosphonic dichloride, obtained in the oxidative chlorophosphonation of 1-chloropropane, we obtained 9.8 g of (V).

Found %: C 38.78, 39.11; H 7.08, 7.04; Cl 17.00. M 213.2. $C_7H_{16}O_3PCl$. Calculated %: C 39.14; H 7.51; Cl 16.52. M 214.64.

3. Diethyl ester of fluoropropanephosphonic acid (VI). Using the conditions of Expt. 1, from 12.3 g (0.07 mole) of fluoropropanephosphonic dichloride, obtained in the oxidative chlorophosphonation of 2-fluoropropane [5], and 100 ml of ethyl alcohol we obtained 5.0 g (VI).

Found %: P 15.16, 15.31; OC_2H_5 44.85, 45.21; M 204.8. $C_7H_{16}O_3PF$. Calculated %: P 15.63; OC_2H_5 45.47, M 198.18.

4. Diethyl ester of 1,2,2-trichloroethanephosphonic acid (VII). Using the conditions of Expt. 1, from 14.0 g (0.056 mole) of 1,2,2-trichloroethanephosphonic dichloride, obtained in the oxidative chlorophosphonation of 1,2-dichloroethylene [2], and 100 ml of ethyl alcohol, we obtained 12.0 g of (VII).

Found %: P 11.63, 11.69; OC_2H_5 32.35, 32.33. $C_6H_{12}O_3PCl_3$. Calculated %: P 11.49; OC_2H_5 33.42

5. Diethyl ester of 1,2-dichloroethenephosphonic acid (XIV). Three grams (0.03 mole) of triethylamine was added to a solution of 10.0 g (0.037 mole) of (VII) in 60 ml of dry ether. After standing for 5 days, the triethylamine hydrochloride was filtered, and we isolated 2.0 g of (XIV).

Found %: C 29.90, 29.60; H 4.50, 4.41; OC_2H_5 37.76, 38.02. $C_6H_{11}O_3PCl_2$. Calculated %: C 30.92; H 4.76; OC_2H_5 38.67.

6. Dipropyl ester of 1,2,2-trichloroethanephosphonic acid (VIII). Using the conditions of Expt. 1, from 10.0 g (0.04 mole) of 1,2,2-trichloroethanephosphonic dichloride and 70 ml of n-propanol we obtained 10.6 g of (VIII).

Found %: C 31.64, 31.47; H 6.46, 6.60; P 10.35. $C_8H_{16}O_3PCl_3$. Calculated %: C 32.32; H 5.42; P 10.41.

7. Diethyl esters of isomeric fluorodichloroethanephosphonic acids (IX). Using the conditions of Expt. 1, from 8.5 g (0.037 mole) of fluorodichloroethanephosphonic dichloride, obtained in the oxidative chlorophosphonation of 1,2-fluorochloroethylene [2], and 50 ml of anhydrous ethyl alcohol, we obtained 8.1 g of (IX).

Found %: C 27.45, 27.13; H 4.57, 4.71; P 11.40, 11.60. $C_6H_{12}O_3PFCl_2$. Calculated %: C 28.47, H 4.78; P 12.24.

Diethyl esters of 2-fluoro-1-chloroethenephosphonic acid (XV) and 2-fluoro-1,2-dichloroethanephosphonic acid (X). Using the conditions of Expt. 5, we obtained 1.7 g of (XV) from 7.5 g of (IX).

Found %: F 8.38; P 14.77. $C_6H_{11}O_3PFCl$. Calculated %: F 8.77; P 14.34.

The (X) that failed to react with triethylamine had:

Found %: C 28.10, 28.58; H 4.99, 4.80; F 7.00; P 11.68, 11.73. $C_6H_{12}O_3PFCl_2$. Calculated %: C 28.47; H 4.77; F 7.51; P 12.24.

9. Dipropyl ester of fluorodichloroethanephosphonic acid (XI). Using the conditions of Expt. 1, from 4.9 g (0.0195 mole) of fluorodichloroethanephosphonic dichloride [2] and 18.0 g (0.3 mole) of n-propanol, we obtained 2.2 g of (XI).

Found %: C 33.19, 33.55; H 5.08; P 10.31. $C_8H_{16}O_3PFCl_2$. Calculated %: C 34.17; H 5.73; P 11.02.

10. Dibutyl ester of 1-chloro-3-butanephosphonic acid (XII). Using the conditions of Expt. 1, from 11.0 g (0.05 mole) of 1-chloro-3-butanephosphonic dichloride, obtained in the oxidative chlorophosphonation of 1-chlorobutane [1], and 30 g of butanol, we obtained 10.9 g of (XII).

Found %: C 50.31, 50.50; H 8.97, 8.98; Cl 12.00, 11.82. $C_{12}H_{26}O_3PCl$. Calculated %: C 50.59; H 9.21; Cl 12.45.

11. Diethyl ester of chlorobromoethanephosphonic acid (XIII). Using the conditions of Expt. 1, from 7.8 g (0.028 mole) of chlorobromoethanephosphonic dichloride, obtained in the oxidative chlorophosphonation of vinyl bromide [2], we obtained 3.9 g of (XIII).

SUMMARY

Some dialkyl esters in the series of halogenated alkane- and alkenephosphonic acids (chloropropane-, fluoropropane-, chlorobutane-, chlorobromoethane-, trichloroethane-, flurodichloroethane-, dichloroethene-, and fluorochloroethenephosphonic) were prepared.

LITERATURE CITED

[1] L. Z. Soborovskii, Yu. M. Zinov'ev and M. A. Englin, Doklady Akad. Nauk SSSR 73, 333 (1950); L. Z. Soborovskii, Yu. M. Zinov'ev and L. I. Muler, Doklady Akad. Nauk SSSR 109, 98 (1956); Yu. M. Zinov'ev and L. Z. Soborovskii, Zhur. Obshchei Khim. 29, 615 (1959). •

[2] L. Z. Soborovskii, Yu. M. Zinov'ev and T. G. Spiridonova, Zhur. Obshchei Khim. 29, 1139 (1959). •

[3] L. Z. Soborovskii, Yu. M. Zinov'ev and M. A. Englin, Doklady Akad. Nauk SSSR 67, 293 (1949).

[4] E. Bergmann and A. Bondi, Ber. 63, 1158 (1930); 66, 286 (1933).

[5] Yu. M. Zinov'ev and L. Z. Soborovskii, Zhur. Obshchei Khim. 29, 2643 (1959). •

•Original Russian pagination. See C. B. translation.

SYNTHESIS AND PROPERTIES OF ALKYLDIFLUOROPHOSPHINES

V. N. Kulakova Yu. M. Zinov'ev and L. Z. Soborovskii

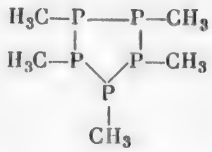
Translated from Zhurnal Obshchei Khimii. Vol. 29, No. 12, pp. 3957–3959, December 1959

Original article submitted November 20, 1958

Alkyl-, aryl-, and dialkylhalophosphines of type $AlkPX_2$, $ArPX_2$, and $(Alk)_2PX$ have been known for a long time [1]: the halogen was usually chlorine, and less frequently, bromine. Methyldiiodophosphine [2] and some perfluoroalkylphosphines [3] were described recently.

In this paper we were able to obtain for the first time some fluoro derivatives of organic phosphines (RPF_2), which can be regarded as being the fluorides of alkylphosphonous acids. These compounds were obtained from the corresponding chloro and iodo derivatives by reacting them with antimony trifluoride under mild conditions.

The obtained compounds of type RPF_2 are unstable substances. When heated or when stored for a long time, they undergo a peculiar transformation, leading, as was shown on the example of methyldifluorophosphine (I), to the formation of substances that, based on the analysis data and molecular weight, we assume to be five-membered cyclic derivatives of phosphorus (VII).



The corresponding alkyltetrafluorophosphines are formed at the same time. The observed transformations can be depicted by the scheme: $10RPF_2 \longrightarrow (RP)_5 + 5RPF_4$.

The preparation of the latter compounds from complexes of composition $RCl \cdot PCl_3 \cdot AlCl_3$ and hydrogen fluoride was described in 1955 [4].

The existence of cyclic compounds containing phosphorus rings was shown by Mahler and Burg [5] in 1957, who reported on the preparation of a four-membered cyclic compound with a composition corresponding to the formula $(CF_3P)_4$. In another paper it was established that the mentioned compound can also exist as the pentamer $(CF_3P)_5$, suffering partial transformation at 250° to the tetramer [6]. However, the cyclic compounds described in the indicated papers were not obtained from alkyldifluorophosphines. As a result, the compound that we synthesized in this paper from the new methyldifluorophosphine is probably the first representative of unsubstituted alkyl phosphorus derivatives with a cyclic structure.

In addition to the unsubstituted alkyldifluorophosphines, we synthesized the corresponding new trifluoromethyl derivatives, CF_3PF_2 (V) and $(CF_3)_2PF$ (VI). The starting materials in this case were the above mentioned iodides [3]. The obtained perfluorides are gaseous compounds that ignite spontaneously in the air. The unsubstituted alkyldifluorophosphines behave in a similar manner.

A characterization of the compounds synthesized by us is given in the table.

TABLE

Compound	Formula	Boiling point	Yield (in %)
I	CH_3PF_2	—28°	35
II	$C_2H_5PF_2$	6—7	22
III	$C_4H_9PF_2$ *	70—71	36
IV	$C_6H_5PF_2$	64—70	14
V	CF_3PF_2	—43—40	64
VI	$(CF_3)_2PF$	—11—8	37
VII	$(CH_3P)_5$ **	123 (2 mm)	96

*d_4^{20} 1.0206. **d_4^{20} 1.1635

EXPERIMENTAL

1. Methylfluorophosphine (I). Into a flask fitted with a reflux condenser and dropping funnel was charged 60 g (0.33 mole) of antimony trichloride and 150 ml of dry benzene, and then 40 g of methyldichlorophosphine was added in drops at such a rate that the temperature of the mixture did not exceed 30°. At the end of addition, the flask was heated on the water bath for 2 hr at 60°. The evolved gases were condensed in a trap cooled with dry ice. The condensate was distilled through a Podbielniak column and we collected 10.1 g of gas. The experiment was run in a nitrogen atmosphere. *

Found %: F 44.7, 44.9. M 86.09. CH_3PF_2. Calculated %: F 45.2. M 84.1.

We also isolated a substance with b.p. 9° (phosphorus methyltetrafluoride).

2. Ethyldifluorophosphine (II). In a manner similar to the above, from 41.6 g (0.31 mole) of ethyldichlorophosphine and 60 g of antimony trichloride, we obtained 6.8 g of (II).

Found %: F 38.12, 38.25. M 100.3. $C_2H_5PF_2$. Calculated %: F 38.76. M 94.08.

We also isolated a substance with b.p. 32—34° (phosphorus ethyltetrafluoride).

3. Butyldifluorophosphine (III). Using the conditions of Expt. 1, but employing toluene as the solvent, we obtained 11.9 g of (III) from 60 g of antimony trichloride and 30 g of butyldichlorophosphine.

Found %: F 29.15, 29.4. $C_4H_9PF_2$. Calculated %: F 30.13.

4. Phenyldifluorophosphine (IV). Using the conditions of Expt. 1, but with dry ether as the medium, we isolated (vacuum distillation) 3.5 g of (IV) from 30 g of phenyldichlorophosphine and 30 g antimony trichloride.

Found %: F 24.95, 25.14. $C_6H_5PF_2$. Calculated %: F 25.99.

5. Trifluoromethyldifluorophosphine (V). A mixture of 2.8 g of trifluoromethyldiiodophosphine and 3 g of antimony trichloride was heated. The evolved gas was condensed in a trap cooled with dry ice. We isolated 0.7 g of (V) from the condensate.

Found %: F 67.52, 68.04. M 140. CPF_5. Calculated %: F 68.84. M 138.

6. Di(trifluoromethyl)fluorophosphine (VI). A mixture of 4.0 g of di(trifluoromethyl)iodophosphine and 4.0 g of antimony trichloride was heated to 40°. We isolated 1.0 g of (VI).

Found %: F 69.96, 70.01. M 195. C_2PF_7. Calculated %: F 70.74. M 188.

Conversion of methyldifluorophosphine to pentamethylcyclopentaphosphine (VII). Two layers were formed when 3.75 g of (I) was heated in a sealed tube for several hours at 35—40°. On distillation, the first to distill was a substance with b.p. 9° (CH_3PF_4). The residue was then vacuum distilled. We collected 0.88 g of (VII).

Found %: C 26.06, 26.15; H 6.81, 6.84. M 226, 236. $C_5H_{15}P_5$. Calculated %: C 26.08; H 6.55. M 230.

Similar transformations were observed when (I) was kept for a long time in sealed tubes at 20°.

SUMMARY

1. The first representatives of the alkyldifluorophosphines (alkylphosphonous difluorides) were prepared.

2. It was postulated that the alkyldifluorophosphines are capable of forming five-membered rings composed of phosphorus atoms.

*All of the subsequent experiments were also run in a nitrogen atmosphere.

LITERATURE CITED

[1] G. M. Kosolapoff, Organophosphorus Compounds (New York, 1950).

[2] V. A. Ginsburg and N. F. Privezentseva, Zhur. Obshchei Khim. 28, 736 (1958). •

[3] F. Bennett, H. Emeleus and R. Haszeldine, J. Chem. Soc. 1565 (1953).

[4] Brit. Patent 734,187 (1955); Chem. Zentr. 5689 (1956).

[5] W. Mahler and A. Burg, J. Am. Chem. Soc. 79, 251 (1957).

[6] Chem. Eng. News 35, 21, 28 (1957).

•Original Russian pagination. See C. B. translation

REACTION OF ETHYLENIMINO-1,4-BENZOQUINONES WITH AMINES

II. REACTION BETWEEN ETHYLENIMINO-1,4-BENZOQUINONES AND PRIMARY AMINES

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Translated from Zhurnal Obshchei Khimii. Vol. 29, No. 12, pp. 3959–3962, December 1959

Original article submitted December 17, 1958

In the previous paper [1] we had shown that the ethylenimino rings of bis(ethylenimino)benzoquinones, in contrast to ethylenimine itself and its C-derivatives, when reacted with secondary amines are smoothly cleaved, with the formation of the corresponding bis(dialkylaminoethylamino)quinones. The only exception proved to be the reaction of piperidine and morpholine with 2,5-bis(ethylenimino)-1,4-benzoquinone, where, besides opening of the ethylenimino ring, a replacement of the ethylenimino moieties by amino radicals was observed. We explained the great ease with which the three-membered rings in ethyleniminoquinones are cleaved as due to an upsetting of the "aromatic" nature of the ethylenimino ring under the influence of the quinoid ring.

In this connection, it seemed of interest to investigate the reaction of ethyleniminobenzoquinones with primary amines. From the literature it is known [2] that ethylenimine and its C-derivatives when reacted with primary amines also suffer cleavage, with the formation of ethylenediamines (the same as when they are reacted with secondary amines) but under more drastic conditions.

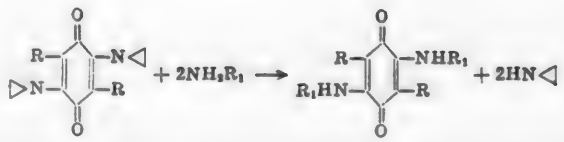
In the present paper we used 2,5-bis(ethylenimino)-, 2-chloro-3,6-bis(ethylenimino)-, 2,5-dichloro-3,6-bis(ethylenimino)-, and 2,5-diethoxy-3,6-bis(ethylenimino)-1,4-benzoquinones as the ethyleniminobenzoquinones, and isopropylamine, cyclohexylamine, benzylamine, and aniline as the primary amines.

Reaction of the ethyleniminoquinones with primary amines was accomplished by refluxing the quinone with excess amine in methyl alcohol. The experimental conditions, as well as the physical properties of the obtained compounds and the analysis results, are given in the table.

As can be seen, when ethyleniminoquinones are reacted with primary amines, there occurs replacement of the ethylenimino groups by the radicals of the primary amines with the formation of the corresponding diaminoquinones. It is interesting that only one ethylenimino group is replaced when 2,5-bis(ethylenimino)-1,4-benzoquinone is reacted with aniline, resulting in the formation of 2-ethylenimino-5-anilino-1,4-benzoquinone. The obtained diaminoquinones are stable, brightly colored compounds that crystallize with ease. The rate with which the ethylenimino groups are replaced by primary amine radicals depends to a large degree on the nature of the substituents in the quinone nucleus. The easiest replacement, with good yields, of the ethylenimino radicals occurs in the case of 2,5-dichloro-3,6-bis(ethylenimino)-1,4-benzoquinone and 2-chloro-3,6-bis(ethylenimino)-1,4-benzoquinone. To displace the ethylenimino groups in 2,5-bis(ethylenimino)-1,4-benzoquinone requires a longer refluxing of the reaction mixture. Regarding 2,5-diethoxy-3,6-bis(ethylenimino)-1,4-benzoquinone, then to complete its reaction with benzylamine requires refluxing the reaction mixture for many hours, and here the yield of reaction product is comparatively small (34%). There is no doubt but that the ease with which the ethylenimino radicals are displaced also depends on the basicity of the primary amines taken for reaction, since in the case of 2,5-bis(ethylenimino)-1,4-benzoquinone and 2,5-dichloro-3,6-bis(ethylenimino)-1,4-benzoquinone the reaction goes much better with isopropylamine ($K_B = 4.3 \times 10^{-4}$), cyclohexylamine or benzylamine ($K_B = 2 \times 10^{-5}$) than with aniline ($K_B = 4.6 \times 10^{-10}$).

TABLE

Reaction of Ethyleniminoquinones with Primary Amines

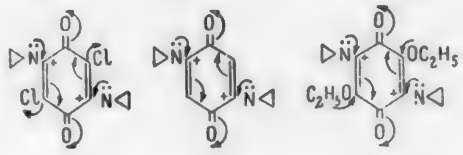


R	R_1	Reaction time (in min)	Yield (in %)	Melting point	Recrystallization solvent	Color of crystals	Found (%)				Calculated (%)			
							C	H	N	Cl	C	H	N	Cl
H	$(CH_3)_2CH$	40	90	240—241°	Methanol—chloroform	Bright red	64.60	7.99	12.55		64.82	8.16	12.61	
H	C_6H_{11}	18	94	239—240	Ethanol	Reddish orange	71.23	8.51	9.26		71.49	8.67	9.27	
H	$C_6H_5CH_2$	10	80	250—251	Methanol--chloroform	Dark red	75.39	5.66	8.94		75.47	5.66	8.80	
H, Cl	$(CH_3)_2CH$	20	63	157—158	Ethanol	Pinkish red	55.86	6.71		13.74	56.13	6.68		13.82
H, Cl	$C_6H_5CH_2$	3	80	207—208		Light red	67.83	5.12			68.08	4.86		
OC_2H_5	$C_6H_5CH_2$	440	34	204—205		Dark green	70.61	6.19			70.90	6.44		
Cl	$(CH_3)_2CH$	30	95	222—223		Cherry-red	49.23	5.69		24.65	49.48	5.54		24.35
Cl	C_6H_{11}	13	93	233—234	Methanol--chloroform	Pink	57.98	6.30	7.48		58.22	6.51	7.55	
Cl	$C_6H_5CH_2$	5	90	222—223 *		Yellow-orange								
Cl	C_6H_5	120	55	285—286 **		Light brown								

*The mixed melting point with authentic 2,5-dibenzylamino-3,6-dichloro-1,4-benzoquinone [3] was not depressed.

**The mixed melting point with authentic 2,5-dianilino-3,6-dichloro-1,4-benzoquinone [4] was not depressed.

The different ease with which bis(ethylenimino)quinones react with primary amines can apparently be explained by the different effect of substituents on the distribution of the electron density in the molecule. When chlorine atoms (a) are present in the ethyleniminoquinone nucleus the electron density near the carbon atoms linked to the ethylenimino rings will be less than for the unsubstituted ethyleniminoquinone (b). This circumstance can facilitate a displacing of the ethylenimino radicals by more basic amines. In contrast, the introduction of ethoxy groups (c) into the ethyleniminoquinone nucleus leads to an increase in the electron density near the carbon atoms attached to the ethylenimino rings, which can hinder a displacement of the ethylenimino radicals.



a b c

EXPERIMENTAL

2,5-Bis(isopropylamino)-1,4-benzoquinone. A suspension of 0.1 g of 2,5-bis(ethylenimino)-1,4-benzoquinone in 0.35 ml of isopropylamine (molar ratio 1:8) and 3 ml of methyl alcohol was refluxed for 40 min until all of the yellow-orange color of the precipitate had changed to a bright red. After two recrystallizations, m.p. 240–241° (from a 1:1 mixture of methyl alcohol and chloroform). Yield 90%. The other experiments were run in the same manner as just described.

2-Ethylenimino-5-anilino-1,4-benzoquinone. A suspension of 0.1 g of 2,5-bis(ethylenimino)-1,4-benzoquinone in 0.35 ml of aniline and 3 ml of methyl alcohol was refluxed for 155 min. Here the solution assumed a dark cherry-red color, while the color of the precipitate changed to a reddish-brown. After two recrystallizations from a mixture of methyl alcohol and chloroform, m.p. 206–207° (decomp.). Yield 80%.

Found %: C 70.10; H 5.30; N 11.67. $C_{14}H_{12}O_2N_2$. Calculated %: C 69.99; H 5.04; N 11.67.

We wish to thank the co-workers in the analytical laboratory of the Institute for performing the analyses.

SUMMARY

1. It was established that the reaction of primary amines with bis(ethylenimino)benzoquinones leads to displacement of the ethylenimino groups by primary amine radicals with the formation of diaminoquinones. Nine new compounds were obtained.

2. It was shown that the ease with which the ethylenimine radicals in ethyleniminoquinones are displaced depends on the nature of the substituents in the quinone nucleus, and also on the basicity of the amines used.

LITERATURE CITED

[1] A. N. Makarova and A. Ya. Berlin, Zhur. Obshchei Khim. 29, 666 (1959). *

[2] U. S. Patents 2,318,729 and 2,318,730; C. A. 37, 5986[1] (1943); G. Coleman and J. Callen, J. Am. Chem. Soc. 68, 2006 (1946); Z. Hicks and G. Coleman, C. A. 42, 4527 (1948); L Clapp, J. Am. Chem. Soc. 70, 184 (1948).

[3] N. P. Buu-Hoï and R. Rover, Rec. trav. chim. 71, 1059 (1952).

[4] M. Niemeyer, Ann. 228, 333 (1885).

*Original Russian pagination. See C. B. translation.

THE HYDROLYSIS OF SOME BIS(2-CHLOROETHYL)AMINES

V. M. Rakova, A. D. Chinaeva and A. Ya. Berlin

Translated from Zhurnal Obshchei Khimii. Vol. 29, No. 12, pp. 3962–3965, December 1959

Original article submitted December 29, 1958

Bis(2-chloroethyl)amines are very interesting in the chemotherapy of cancer. W. Ross [1] makes the statement that those bis(2-chloroethyl)amines which are easily hydrolyzed possess biological activity. It seemed of interest to study the hydrolysis of some bis(2-chloroethyl)amines for the purpose of comparing the ease of hydrolysis with their tumor-inhibitory action. The following compounds were examined: DL-p[bis(β-chloroethyl)amino]-phenylalanine hydrochloride (Sarcolysin), 4-methyl-5-[bis(β-chloroethyl)amino]uracil (Dopan), 2,2'-dichloro-N-methyl-diethylamine N-oxide hydrochloride (Nitromin), methyl(2-chloroethyl)-(2-chloropropyl)amine hydrochloride (Embichin 11), D-1,6-bis(2-chloroethylamino)-1,6-didesoxymannitol dihydrochloride (Degranol or BCM), methyl-bis(2-chloroethyl)amine hydrochloride (Embichin I), DL-m[bis(β-chloroethyl)amino]phenylalanine hydrochloride (Metasarcolysin) and N,N-bis(2-chloroethyl)aniline hydrochloride (Lymphochin). We took 50% ethyl alcohol as the solvent, since all of the investigated compounds are soluble in it. The hydrolysis was run at 50°, and the concentration of the different compounds was taken equal to 0.5853×10^{-3} molar. The chloride ion was determined by titration with 0.01 N mercury nitrate solution in the presence of diphenylcarbazone.

The hydrolysis curves obtained for the investigated compounds are shown in Fig. 1. Here it should be mentioned that in the experiment with Dopan, not containing a molecule of HCl as the salt, we added an equivalent amount of HCl to the solution in advance. On the other hand, in the case of Degranol the solution originally contained 2 moles of HCl. Consequently, to obtain more comparable results, the initial point on the hydrolysis curve of each compound was established by subtracting that amount of chloride ion which corresponded to the amount of hydrochloride present. As can be seen from Fig. 1, all of the compounds show some slowing up of the hydrolysis process with time, which can be due to one of the following reasons.

1. The chlorine atoms in the two 2-chloroethyl groups hydrolyze in succession, in which connection the first chlorine atom, found in the bis(2-chloroethyl)amine, is cleaved at a more rapid rate than the second chlorine atom, found in the (2-chloroethyl)-(2-hydroxyethyl)amine molecule.

2. The chlorine atoms in bis(2-chloroethyl)amines hydrolyze simultaneously, in which connection a decrease in the hydrolysis rate is explained by a gradual accumulation of chloride ions, which hinder the first stage of the hydrolysis process, associated with the formation of carbonium ion [2].

If the second reason is accepted, then adding 2 equiv. of chloride ion to the solution before hydrolysis should cause the hydrolysis rate to be retarded at the very start to that degree where it is approximately equal to the rate corresponding to the slope of the terminal segment of each curve (broken line in Fig. 2). However, experiment revealed that although the hydrolysis of Sarcolysin is retarded when the solution contains 2 equiv. of added NaCl, still the retardation is much less than if the above reason held. At the same time, dissolving Sarcolysin at a temperature close to 50° (60°), but in a physiological solution (0.85% NaCl), as is done when studying the general biological and tumor-inhibitory action of compounds, is not accompanied by noticeable hydrolysis. Consequently, although small concentrations of chloride ions retard the hydrolysis of Sarcolysin only slightly, still in larger amount they exert a sharply retarding effect.

On the other hand, based on our data, when Sarcolysin is dissolved in water at 60°, the amount of chloride ions formed within 5 min is already about 50% of the total amount of chlorine present in the bis(2-chloroethyl)-

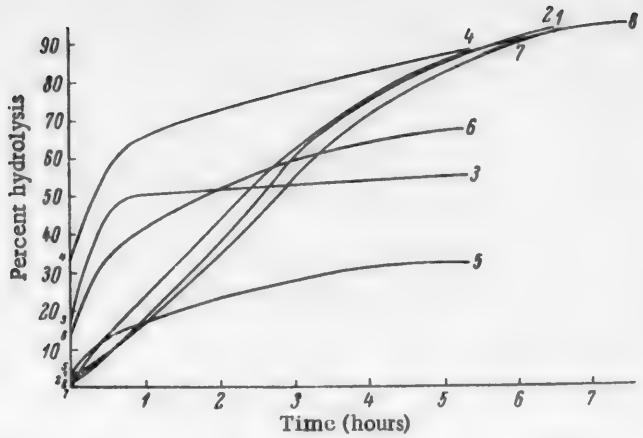


Fig. 1. Curves for hydrolysis of bis(2-chloroethyl)amines.

1) Sarcolysin; 2) Dopan (+ 1 equiv. HCl); 3) Nitromin; 4) Embichin 11; 5) Degranol; 6) Embichin; 7) Metasarcolysin; 8) Lymphochin.

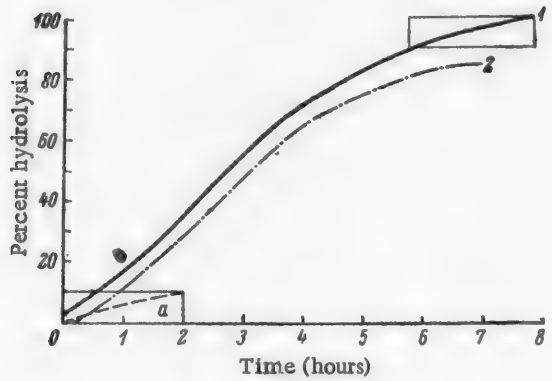


Fig. 2. Curve for the hydrolysis of Sarcolysin in aqueous alcohol (1) and in a solution containing 2 equiv. NaCl (2).

a) Terminal segment of the curve for the hydrolysis of Sarcolysin arbitrarily transferred to the start of the process.

amino group. In like manner, if Sarcolysin is dissolved in water at 60°, the solution cooled rapidly, and then sufficient NaCl is added to create the concentration of the physiological solution, then in this case no biological effect whatsoever is observed.* The negative results obtained in the biological testing of such a solution serve as evidence that the hydrolysis of Sarcolysin proceeds with the formation of hydroxychloro compounds of type Cl—CH_2—CH_2—N—(R)—CH_2—CH_2OH, since in the opposite case, the presence of even half of the taken amount of Sarcolysin should have been manifested in the corresponding degree of biological activity. As a result, the experimental data that we obtained for Sarcolysin support the statement made above that in the hydrolysis of bis(chloroethyl)amines, the cleavage of the chlorine atoms from the two chloroethyl groups proceeds for the most part in a consecutive manner.

*Established by G. L. Zhdanov in the Laboratory of Experimental Chemotherapy of our Institute.

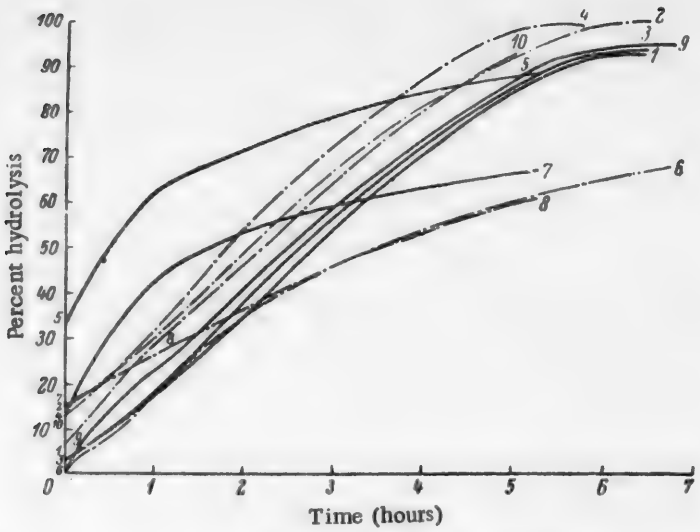


Fig. 3. Curves for the hydrolysis of bis(2-chloroethyl)amines in aqueous alcohol and with the addition of two equivalents of HCl.

1) Sarcolysin; 2) Sarcolysin (+ 2 equiv. HCl); 3) Dopan; 4) Dopan (+ 2 equiv. HCl); 5) Embichin 11; 6) Embichin (+ 2 equiv. HCl); 7) Embichin; 8) Embichin (+ 2 equiv. HCl); 9) Lymphochin; 10) Lymphochin (+ 2 equiv. HCl).

The consecutive manner in which chlorine ions are formed in bis(2-chloroethyl)amines is typically expressed in the curves for the hydrolysis of aliphatic amines, especially for the case of Nitromin, coinciding with those described in the literature [3]: one chlorine ion is formed rapidly, and then the hydrolysis curve changes its direction sharply, and the cleavage of the second chlorine atom proceeds at a much slower rate. The above mentioned fact (Fig. 1) that chlorine ions are formed at a rapid rate in the initial stages of the hydrolysis of aliphatic chloroethylamines undoubtedly corresponds to the stage of forming ethylenimonium ions [4].

Our research on the matter is being continued.

SUMMARY

1. The hydrolysis of some bis(2-chloroethyl)amines in 50% ethyl alcohol at 50° was investigated.

2. It was shown that the addition of chloride ions retards the hydrolysis of 2-chloroethyl groups.

3. Some theories were expressed regarding the manner in which these compounds hydrolyze.

LITERATURE CITED

[1] W. Ross, Ann. N.Y. Acad. Sci. 68 669 (1958).

[2] W. Ross, Advances in the Study of Cancer 1 [Russian translation] (Moscow, 1955), p. 521.

[3] N. Brock, Z. Krebsforschung 62, 9 (1957).

[4] W. E. Hanby, G. S. Hartley, E. O. Powell and H. N. Rydon, J. Chem. Soc. 519 (1947).

SYNTHESIS OF CITRAL AND ITS ANALOGS

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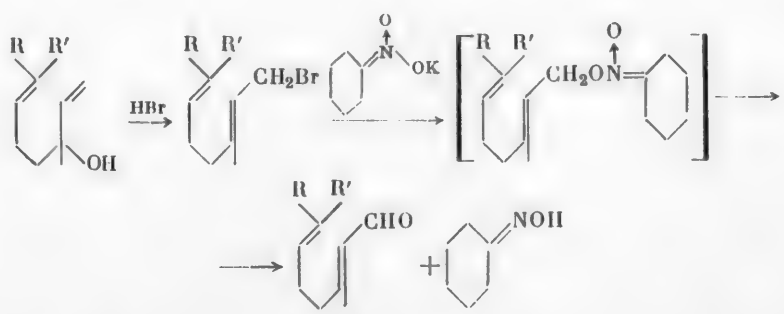
Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3965-3968, December, 1959

Original article submitted October 31, 1958

Citral is the basic intermediate in the synthetic production of α- and β-ionones, vitamin A, and β-carotene. The analogs of citral possess great interest for the synthesis of the corresponding analogs of the above-mentioned natural products. At the present time citral is produced mainly by the oxidation of coriander oil. The most practical synthetic method for the preparation of citral would be the oxidation of linalool. However, this method enables obtaining citral in a yield of only 42% [1].

A number of interesting attempts to synthesize citral by the oxidation of geranyl halides, which are easily obtained by reacting linalool with either hydrogen halide acids or phosphorus halides, and also employing the telomerization reaction [2], are reported in the literature. Sommelet was the first to accomplish this transformation by decomposing the urotropine complex of the geranyl halide [3]. A detailed study was made of this reaction, but despite various modifications, the yield of citral does not exceed 40%, based on the geranyl halide [2]. Mention should also be made of the method in which geranyl bromide is converted to citral by the oxidation of its pyridine complex with p-nitrosodimethylaniline [4]. The yield of citral by this method is 20%. Recently, the aci-form of 2-nitropropane [5] was used to oxidize primary allylic halides to aldehydes. Citral, 3-methylcitral, and some polyenic aldehydes were obtained in good yield using this method.

In this paper we investigated the synthesis of citral and a number of its analogs, using the commercially available nitrocyclohexane. Linalool and its analogs, needed to accomplish the mentioned reactions, were obtained by a method that was developed in our laboratory, which consisted in the condensation of methylheptenone and its analogs with acetylene under pressure, followed by selective hydrogenation of the obtained acetylenic alcohols [6]. The tertiary ethylenic alcohols obtained in this manner were easily converted to the corresponding primary bromides of allylic type by reaction with dry hydrogen bromide at a temperature ranging from −5 to +10°. The thus obtained bromides, without prior distillation, were then reacted with the potassium salt of nitrocyclohexane in aqueous alcohol medium. The intermediately formed nitronic ester is unstable and immediately decomposes into aldehyde and cyclohexanone oxime. The mechanism of the reaction is depicted by the following scheme:



The obtained aldehydes were purified through the bisulfite compounds. Geranyl chloride and its analogs can also be used successfully in this reaction. The constants of the citral and its analogs, obtained by the indicated method, are given in the table.

For most of the aldehydes, the yield based on the tertiary alcohol ranged from 60 to 80%, with the exception of 3-methyl-2,6-octadien-1-al (II) and 7-chloro-3-methyl-2,6-octadien-1-al (III), which proved to be unstable in alkaline medium and were obtained in 35-39% yield. 3,7,8,8-Tetramethyl-2,6-nonadien-1-al (IV) was also obtained by us in 50% yield using 2-nitropropane.

In the present paper we also investigated the direct oxidation of geranyl bromide (and geranyl chloride) using sodium dichromate in alkaline medium. The yield of citral after purification through the bisulfite compound was 21%.

The UV-absorption spectra of the obtained citral and its analogs display an intense absorption band at 228-229 mμ and a less intense absorption band at around 324 mμ, which is characteristic for this type of compound [7].

Evaluation of the obtained citral analogs as perfumes revealed that 7-chloro-3-methyl-2,6-octadien-1-al (III) and 3,7-dimethyl-2,6-nonadien-1-al (IV) have an odor that closely resembles natural citral. A disagreeable fatty odor increases in intensity for compounds (V), (VI), and (VII). Compound (II) has a disagreeable odor, having nothing in common with the odor of citral.

EXPERIMENTAL

Citral. a) Geranyl bromide. Linalool (27.8 g) was saturated with 16.5 g of dry hydrogen bromide at −5°. The reaction mass was allowed to stand for 3 hr at room temperature. The obtained geranyl bromide was separated from the water and used without prior distillation in subsequent reactions.

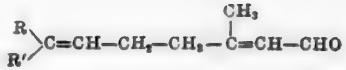
b) Citral. Nitrocyclohexane (32.5 g) was added in drops to a solution of 14 g of KOH, 25 ml of water and 140 ml of isopropyl alcohol at 20°. The mixture was stirred for 15 min, and then the above-obtained geranyl bromide was added. The reaction temperature was maintained at 50-60° for about 20 min by external cooling. The stirring was continued for another 20 min at 50-30°, and then the reaction product was poured into 500 ml of cold water and extracted with ether. The ether extract was washed several times with 5% sodium hydroxide solution and water. The ether was evaporated, while the residual citral was added in 30 min to a solution of 105 g of sodium bisulfite, 37.5 g of sodium bicarbonate, and 600 ml of water, and the mixture was stirred for 6 hr at 20°. The upper oil layer was extracted with ether, while the water solution of citral bisulfite compound was decomposed with 20% sodium hydroxide solution. The liberated citral was extracted with toluene, washed with water, and vacuum distilled. We obtained 22 g of citral with b. p. 112-113° (16 mm).

In a similar manner we obtained: 3-methyl-2,6-octadien-1-al (II); 2,4-dinitrophenylhydrazone, m. p. 139-140°; 7-chloro-3-methyl-2,6-octadien-1-al (III); 3,7-dimethyl-2,6-nonadien-1-al (IV); 3,7,8-trimethyl-2,6--nonadien-1-al (V); 3,7,8,8-tetramethyl-2,6-nonadien-1-al (VI); and 3,8-dimethyl-7-isopropyl-2,7-nonadien-1--al (VII). (The constants and yields are given in the table.)

Previously these compounds had been obtained from methylheptenone and its analogs using ethoxyacetylene [8].

3,7,8,8-Tetramethyl-2,6-nonadien-1-al (VI). a) Bromide. 3,7,8,8-Tetramethyl-1,6-nonadien-3-ol (35.3 g) was saturated with dry hydrogen bromide to a weight increase of 15.3 g (5% excess HBr). The mixture was allowed to stand overnight. Ether was added to the mixture, the water layer was separated, the product washed with water, the ether removed under slight vacuum, and the obtained bromide used without prior distillation in subsequent reactions.

b) Aldehyde (VI). 2-Nitropropane (19.6 g) was added in drops to a solution of 13.8 g of KOH in 22 ml of water and 140 ml of isopropyl alcohol at such a rate that the temperature of the mixture did not exceed 20°, and then the above-obtained bromide was added. After adding the bromide, the temperature of the reaction mass was raised to 40-45°. The mixture was stirred at this temperature for 20 min and then it was poured into 0.5 liter of cold water. The aldehyde was extracted with ether, and the ether extract was washed with 1% sodium hydroxide solution and water. The ether was evaporated, and the aldehyde was purified through the bisulfite compound, the same as described in the preceding experiment. We obtained 17.2 g (50%) of 3,7,8,8-tetramethyl-2,6-nonadien-1--al (VI) with b.p. 80° (0.2 mm) and n_D^{20} 1.4835.



№	R	R′	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	λ max (in mμ)	ϵ_{max}	Found (%) C	Found (%) H	Calculated (%) C	Calculated (%) H	Yield (in %)
(I)	CH_3	CH_3	117—119° (20)	1.4863	0.8995	48.60	47.46	238, 324	13500, 65	—	—	—	—	80
(II)		H	72—73 (3)	1.4846	0.8923	44.37	42.84	239, 322	16440, 56.2	78.13, 78.30	10.51, 10.44	78.21	10.21	35
(III)		Cl	90—92 (2.5)	1.5042	1.0414	49.11	47.71	239, 326.5	14300, 77	62.83, 62.82	7.50, 7.41	62.61	7.59	39
(IV)		C_2H_5	96—97 (4)	1.4860	0.8888	53.64	52.07	239	12400	79.41, 79.29	10.92, 11.01	79.52	10.84	62
(V)		iso-C_3H_7	98—99 (3)	1.4838	0.8853	58.25	56.69	238.5	14210	79.94, 79.81	11.17, 11.09	79.94	11.18	64
(VI)		tert-C_4H_9	80—82 (0.2)	1.4840	0.8841	62.40	61.31	239	14750	80.19, 80.28	11.37, 11.49	80.41	11.34	59
(VII)	iso-C_3H_7	iso-C_3H_7	84—85 (0.02)	1.4808	0.8807	67.28	65.99	238, 321	14600, 62.2	80.53, 80.38	11.62, 11.67	80.71	11.62	61.5

Oxidation of geranyl chloride with sodium dichromate. Into a three-necked flask fitted with a stirrer, condenser, and thermometer, was charged 52 g of geranyl chloride, 5.5 g of anhydrous sodium carbonate, and 28 g of sodium dichromate in 150 ml of water. The mixture was heated with vigorous stirring for 10 hours. The reaction product was steam distilled and then extracted with ether. The ether extract was dried over magnesium sulfate. On distillation we obtained 19 g of compound with b. p. 54-57° (0.15 mm) and n_D^{20} 1.4749. The compound was purified through the bisulfite compound, the same as described above. We obtained 10 g (21%) of citral with b. p. 103-104° (10 mm) and n_D^{20} 1.4884, and having the characteristic odor of lemon rind.

SUMMARY

A method was developed for obtaining citral and its analogs by the oxidation of geranyl halides and the corresponding analogs, using nitrocyclohexane.

LITERATURE CITED

[1] M. Stoll and A. Commarmont, Helv. Chim. Acta 32, 1354 (1949).

[2] K.V. Leets, A. K. Shumeiko, A. A. Rozner, I. V. Kudryavtseva, and A. I. Pilyavskaya, Zhur. Obshchei Khim. 27, 1510 (1957).*

[3] M. Sommelet, Compt. rend. 157, 852 (1913).

[4] P. Karrer and A. Epprecht, Helv. Chim. Acta 24, 1039 (1941).

[5] O. Isler and co-workers, Helv. Chim. Acta 40, 1250 (1957).

[6] I. N. Nazarov and co-workers, Doklady Akad. Nauk SSSR 114, 796 (1957).*

[7] L. K. Evans and A. E. Gillam, J. Chem. Soc. 565 (1943).

[8] I. N. Nazarov, Zh. A. Krasnaya, and V. P. Vinogradov, Zhur. Obshchei Khim. 28, 460 (1958).*

*Original Russian pagination. See C. B. translation.

INVESTIGATION IN THE FIELD OF SYNTHESIS OF STEROID-HORMONE ANALOGS

VIII. SYNTHESIS OF ANTI-TRANS- ANTI-CIS- AND SYN-CIS-3-(p-ANISYL)-1-METHOXYCYCLOPENTANE-2-ACETIC ACIDS

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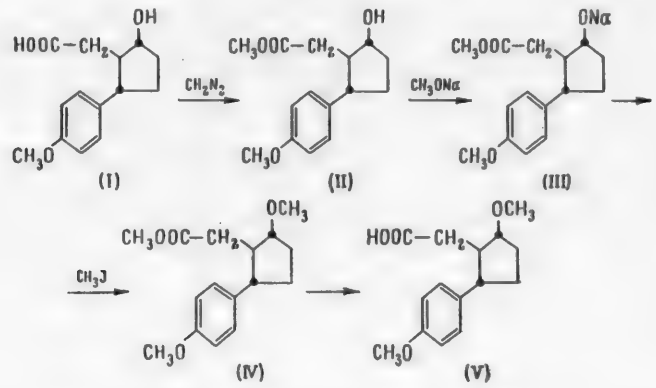
Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3969-3971, December, 1959

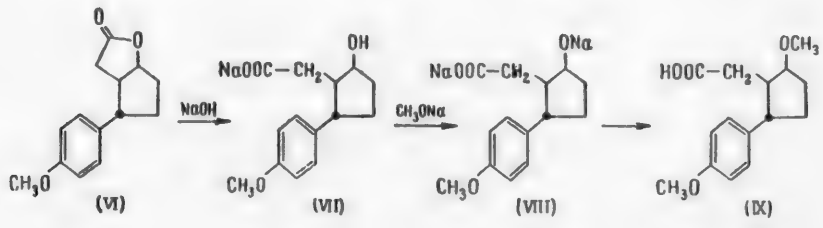
Original article submitted November 28, 1958

We synthesized anti-trans-methoxy acid (V) in accordance with the following scheme:



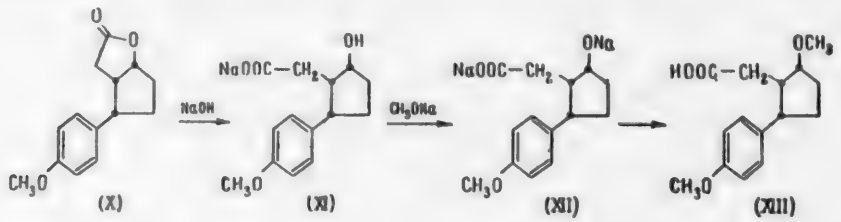
On treatment of the methyl ester of hydroxy acid (II) with sodium methoxide there was obtained alkoxide (III), which, when heated with methyl iodide, formed methyl ether (IV) in 70-77% yield. This yield of the ether was obtained only in the case where the methanol, evolved on treatment of hydroxy compound (II) with sodium methoxide, was completely driven off with a large amount of dry benzene.

We prepared anti-cis-methoxy acid (IX) from anti-cis-hydroxy acid lactone (VI).



Disodium derivative (VIII) was prepared by treating the lactone first with an equivalent quantity of sodium hydroxide and then with an equivalent quantity of sodium methoxide, followed by completely distilling off the methanol with benzene. When disodium derivative (VIII) was treated with methyl iodide, anti-cis-methoxy acid (IX) was obtained in 31% yield.

Syn-cis-methoxy acid (XIII) was similarly prepared from syn-cis-hydroxy acid lactone (X) in 48% yield.



EXPERIMENTAL

1. Anti-trans-3-(p-methoxyphenyl)-1-methoxycyclopentane-2-acetic acid (V).

a) Methyl anti-trans-3-(p-methoxyphenyl)cyclopentan-1-ol-2-acetate (II). To a cooled solution of 15 g of anti-trans-hydroxy acid (I) in 30 ml of methanol was added 500 ml of an ethereal solution of diazomethane (about 13 g). The reaction mixture was left to stand for 24 hours at room temperature. The excess diazomethane was driven off in vacuo. The ethereal solution was washed with 5% sodium carbonate solution and water, and dried. After driving off the ether there was obtained 15.1 g (95%) of anti-trans-hydroxy acid methyl ester (II) in the form of an oil; the latter was used without further purification in the next step.

b) Methyl anti-trans-3-(p-methoxyphenyl)-1-methoxycyclopentane-2-acetate (IV). To a sodium methoxide solution, prepared from 1.32 g of sodium and 60 ml of methanol, was added a solution of 15.1 g of anti-trans-hydroxy acid methyl ester (II) in 200 ml of dry benzene, with stirring. Then the benzene-methanol mixture was slowly distilled off in a current of nitrogen. For more complete removal of the methanol, 200 ml of dry benzene was added and the evaporation repeated. This operation was repeated twice. Then 200 ml of benzene and 25 ml of methyl iodide were added and the mixture boiled until an alkaline reaction was no longer obtained (16 hours). The benzene solution was washed with water and dried. After solvent removal there was obtained 14.3 g of a mixture of methoxy acid methyl ester (IV) and hydroxy acid methyl ester (II), which was chromatographed on 300 g of aluminum oxide. A 12.2g quantity (76.8%) of methoxy acid methyl ester (IV) was eluted with benzene. A 1.6 g quantity (10.6%) of the original methyl ester (II) was eluted with a 10% solution of ethyl acetate in benzene.

c) Methyl anti-trans-methoxyacetate (IV) was hydrolyzed by boiling 12.2 g of ester (IV) with 200 ml of 5% methanolic potassium hydroxide solution for one-half hour. After driving off the methanol in vacuo, the residue was dissolved in water. The aqueous solution was extracted with ether and acidified. The resulting precipitate of the acid was filtered out and washed on the filter with water. There was obtained 9.4 g of anti-trans-methoxy acid (V), m. p. 92-92.5° after recrystallization from ether. The yield of acid (V), if the recovered hydroxy acid methyl ester (IV) is taken into account, was 69.5%.

Found %: C 68.09; $C_{15}H_{20}O_4$. Calculated %: C 68.16; H 7.63

2. Anti-cis-3-(p-methoxyphenyl)-1-methoxycyclopentane-2-acetic acid (IX).

a) Anti-cis-hydroxy acid sodium salt (VII) was prepared from lactone (VI),* m. p. 141-142°, and an equivalent quantity of sodium hydroxide (5% solution). After driving off the water in vacuo, the white, crystalline residue was dried over phosphorus pentoxide.

b) To a sodium methoxide solution, prepared from 1.24 g of sodium and 60 ml of methanol, was added a suspension of 14.5 g of sodium salt (VII) in 200 ml of dry benzene. The benzene-methanol mixture was distilled

* See Zhur. Obshchei Khim. 28, 832 (1958) [C. B. translation].

off; 200 ml of benzene was added and distilled off in turn. The operation was repeated twice. Then 200 ml of benzene and 25 ml of methyl iodide were added and the mixture boiled for 16 hours. The reaction mass was washed with water. The aqueous extract was acidified. The resulting oily precipitate was extracted with chloroform. The chloroform extract was washed with 5% sodium carbonate solution. On acidification of this solution a precipitate formed, which was filtered out and washed with water. There was obtained 4.4 g (31%) of anti-cis-methoxy acid (IX), m. p. 81.5-82.5°.

Found %: C 68.08; H 7.61. $C_{15}H_{20}O_4$. Calculated %: C 68.16; H 7.63.

A 6.9 g quantity (56%) of the original lactone was obtained from the chloroform extract.

3. Syn-cis-3-(p-methoxyphenyl)-1-methoxycyclopentane-2-acetic acid (XIII).

To a sodium methoxide solution, prepared from 2 g of sodium and 80 ml of methanol, was added a suspension of 23.25 g of syn-cis-hydroxy acid sodium salt (XI) in 250 ml of dry benzene. Sodium salt (XI) was prepared from syn-cis-hydroxy acid lactone (X) as described above for anti-cis-hydroxy acid sodium salt (VII). The reaction was carried out under the conditions described for the preparation of anti-cis-methoxy acid (IX). After similar treatment there was obtained 10.85 g (48%) of the syn-cis-methoxy acid, m. p. 94-95° (from ether).

Found %: C 67.95; H 7.40. $C_{15}H_{20}O_4$. Calculated %: 68.16; H 7.63.

SUMMARY

Anti-trans-, anti-cis-, and syn-cis-3-(p-methoxyphenyl)-1-methoxycyclopentane-2-acetic acids, which are not described in the literature, have been synthesized.

INVESTIGATION IN THE SERIES OF N-SUBSTITUTED INDAZOLES

IV. SYNTHESIS OF DERIVATIVES OF N-INDAZYLALIPHATIC ACIDS•

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3971-3977,

December, 1959

Original article submitted November 24, 1958

Recently [1] it was found that isonicotinothioamide has antitubercular activity both with respect to common strains of Mycobacterium tuberculosis and with respect to strains resistant to isoniazid, streptomycin, and PASK § [2]. α-Alkylisonicotinothioamides have even greater activity [3]. Certain other heterocyclic acid thioamides, e.g., 2-indolycarbothioamide, also were found to be tuberculostatic [4].

In connection with this, the synthesis of thioamides in the indazole series was of definite interest. In the present article, the preparation and properties of N-indazylaceto- and N-indazylpropiothioamides are described.

We synthesized derivatives of indazylacetic acid, proceeding from ethyl indazyl-2-acetate prepared by the Auwers method [5]. Treatment with concentrated aqueous ammonia solution in the presence of alcohol gave the corresponding amide†, which was converted to the nitrile by treatment with phosphoryl chloride in pyridine solution. When hydrogen sulfide was passed into a solution of the nitrile in alcoholic ammonia, indazyl-2-acetothioamide was formed. 6-Nitroindazylacetamide, 6-nitroindazylacetonitrile, and ethyl 6-nitroindazylacetate were obtained in accordance with the same scheme. 6-Nitroindazylacetothioamide could not be obtained, since the reaction of the nitrile with hydrogen sulfide was accompanied by pronounced tarring and the evolution of a large amount of sulfur.

Although ethyl 6-nitroindazylacetate has long been known, it was not known whether this ester was the 1- or 2-isomer. By comparing the ultraviolet spectrum‡ of the nitrile obtained from this ester thru the amide, with the spectra of 1- and 2-methyl-6-nitroindazoles, we showed that this nitrile has the same structure as 1-methyl-6-nitroindazole. Therefore, the original ester also is 1-substituted (see Fig. 1).

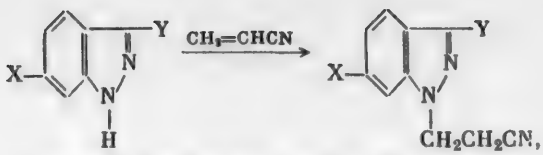
The starting materials for preparing β-indazylpropiothioamide and its 3- and 6-derivatives were the corresponding nitriles, which we prepared by the cyanoethylation of indazole and 3-chloro-, 6-amino-, and 6-nitroindazoles with acrylonitrile in the presence of an alcoholic solution of trimethylphenylammonium ethoxide [7], in tertiary butyl alcohol at 40-43°.

•For article III see Zhur. Obshchei Khim. 29, 3720 (1959) [C. B. translation].

§ Listed as Paskate in American Drug Index.

† After we had completed this work, a description of an analogous method of preparing indazyl-2-acetamide and -acetonitrile appeared in the literature [6].

‡ All spectra were taken in the VNIKhFI physical chemistry laboratory under the direction of Yu. N. Sheinker; for this the authors express their thanks.



where X, Y = H, H; NO_2, H; NH_2, H; H, Cl.

On cyanoethylation of 6-aminoindazole under the conditions indicated above, only one acrylonitrile molecule is added. Since aromatic amines are cyanoethylated with much greater difficulty [8], it was to be expected that under our conditions the imino group of the indazole nucleus would be cyanoethylated.

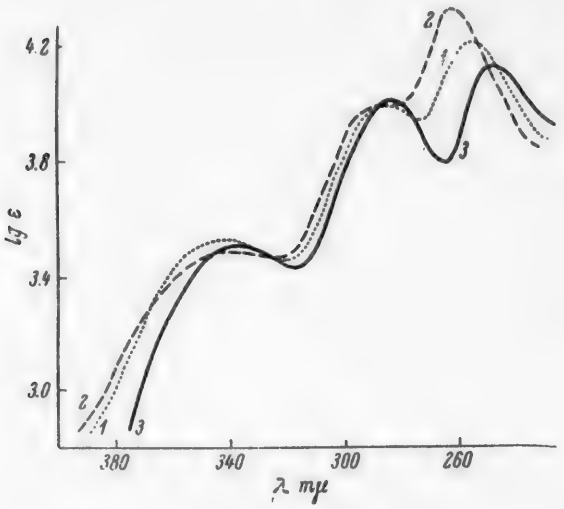


Fig. 1. Ultraviolet spectra. 1) 1-Methyl-6-nitro-indazole; 2) 2-methyl-6-nitroindazole; 3) 6-nitroindazyl-1-acetonitrile.

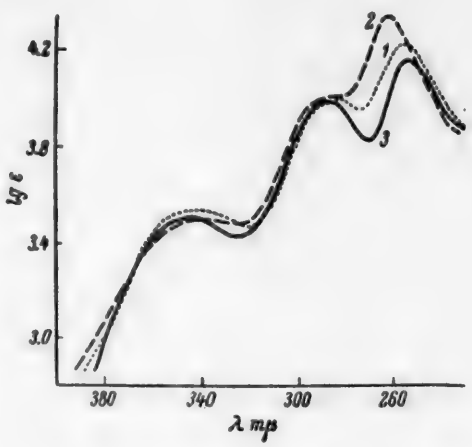
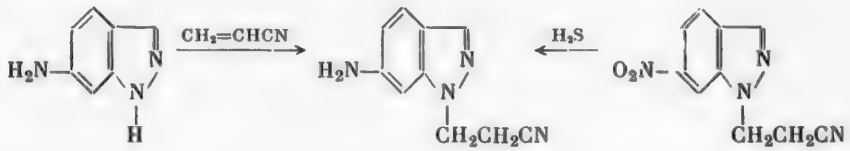


Fig. 2. Ultraviolet spectra. 1) 1-Methyl-6-nitroindazole; 2) 2-methyl-6-nitroindazole; 3) 6-nitroindazyl-1-propionitrile.

The structure of the resulting β-(6-aminoindazyl) propionitrile was confirmed by preparing the same compound through reduction with hydrogen sulfide of β-(6-nitroindazyl) propionitrile, the strucutre of which was proved spectroscopically.



β-Indazyl-1-propionitrile and its 3- and 6-derivatives gave the corresponding thioamides on treatment with hydrogen sulfide.

It is interesting to note that both indazole [9] and all substituted indazoles studied by us, regardless of the nature of the substituents, form the corresponding 1-derivatives on cyanoethylation, as was proved by comparing their ultraviolet spectra with the spectra of the correspondingly substituted 1- and 2-methylindazoles (see Figs. 2 and 3).

We also investigated the ultraviolet spectra of 3-chloroindazole and 6-nitroindazole and showed that these compounds, as well as unsubstituted indazole [9], have a benzoid structure (see Figs. 4 and 5).

The substances obtained by us were tested for antibacterial action.* Certain thioamides have tuberculostatic activity; e.g., β-(indazyl-1)-propiothioamide inhibits the growth of the tuberculosis bacillus in a dilution of 1:64,000. Introduction of chlorine in position 3 of the indazole nucleus enhances the activity. Thus, β-(3-chloroindazyl-1)-propiothioamide inhibits the growth of tuberculosis bacilli of the human-type strain H-37-Rv in a dilution of 1:2,000,000 in the absence of serum, or 1:64,000 in its presence.

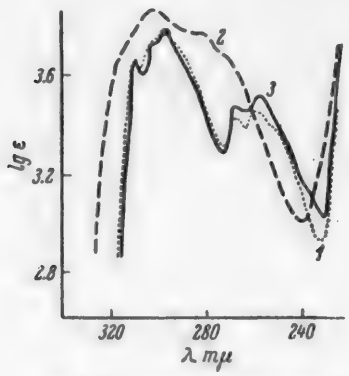


Fig. 3. Ultraviolet spectra. 1) 1-Methyl-3-chloroindazole; 2) 2-methyl-3-chloroindazole; 3) 3-chloroindazyl-1-propionitrile.

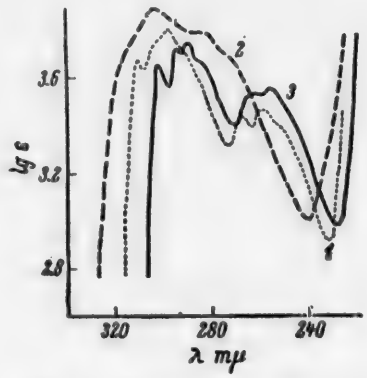


Fig. 4. Ultraviolet spectra. 1) 1-Methyl-3-chloroindazole; 2) 2-methyl-3-chloroindazole; 3) 3-chloroindazole.

EXPERIMENTAL

2-Indazylacetamide. A mixture of 1.63 g of ethyl 2-indazylacetate, 5 ml of alcohol, and 10 ml of concentrated ammonia solution (d 0.9) was shaken for 40 hours. The resulting precipitate was filtered out and washed with water. There was obtained 1.25 g (89.5%) of 2-indazylacetamide, m. p. 202-203°. After recrystallization from water, this consisted of colorless needles with m. p. 203°, very soluble in hot alcohol and hot water, less soluble in cold alcohol and acetone, and insoluble in ether and benzene.

Found %: C 61.44; H 5.21; N 24.15. $C_9H_9ON_3$. Calculated %: C 61.70; H 5.18; N 23.98.

2-Indazylacetonitrile. To a suspension of 0.88 g of 2-indazylacetamide in 2 ml of dry pyridine, 0.92 g of phosphoryl chloride was slowly added dropwise during 10 minutes, with stirring. In this case the mixture turned red, the precipitate dissolved, and the temperature rose to 50-70°. The reaction mass was stirred for 1 hour more at room temperature. It was then dissolved in 10 ml of cold water and acidified to Congo with hydrochloric acid. The acid solution was extracted with ether. The ethereal solution was dried with sodium sulfate, charcoal being added, and evaporated. There was obtained 0.46 g of a substance with m. p. 72-75°. After recrystallization from a benzene-n-heptane mixture (2:1), 2-indazylacetonitrile consisted of colorless prisms with m. p. 81-82°, readily soluble in ether, alcohol, benzene, and chloroform, and slightly soluble in water.

Found %: C 68.56; H 4.48; N 26.36. $C_9H_7N_3$. Calculated %: C 68.78; H 4.49; N 26.74

2-Indazylacetothioamide. Into a solution of 0.52 g of 2-indazylacetonitrile in 10 ml of saturated alcoholic ammonia solution (at room temperature), a current of dry hydrogen sulfide was passed for 3 hours. In this case a white precipitate formed within 40 minutes. The mixture was left at room temperature for 4 days. Then the precipitate was filtered out, washed with water, and dried. There was obtained 0.61 g of a substance with m. p. 185° (decomp.). After recrystallization from 80% alcohol, 2-indazylacetothioamide had m. p. 200-201° (decomp.); colorless prisms, very soluble in dioxane, less soluble in acetone, hot alcohol, and hot ethyl acetate, and almost insoluble in benzene, ether, and chloroform.

*The biological investigation was carried out in the Chemotherapy Division of VNIKhFI under the direction of G. N. Pershin; for this the authors express their thanks.

Found %: 56.62, 56.62; H 4.81, 4.73; N 21.84, S 16.43. $C_9H_9N_3S$. Calculated %: C 56.53; H 4.74; N 21.97; S 16.77.

6-Nitroindazyl-1-acetamide was obtained, like 2-indazylacetamide, from ethyl 6-nitroindazyl-1-acetate in 96.5% yield; colorless prisms with m. p. 208° (from 35% aqueous alcohol); very soluble in hot alcohol and hot acetone, less soluble in cold alcohol, and insoluble in ether and benzene.

Found %: C 48.90; H 3.35; N 25.61. $C_9H_8O_3N_4$. Calculated %: C 49.09; H 3.66; N 25.45.

6-Nitroindazyl-1-acetonitrile was obtained by the same method as 2-indazylacetonitrile. Yield 85%. 6-Nitroindazyl-1-acetonitrile consisted of yellow pellets (from 50% aqueous alcohol) with m. p. 149-150°, readily soluble in ethyl acetate, benzene, chloroform, and ether, and less soluble in alcohol. By comparing the ultraviolet spectrum of this substance with the spectra of 1- and 2-methyl-6-nitroindazoles, its structure was found to be that of the 1-isomer (see Fig. 1).

Found %: C 53.46; H 3.04; N 27.35; $C_9H_6O_2N_4$. Calculated %: C 53.47; H 2.99; N 27.71.

β-(Indazyl-1)-propionitrile. To a suspension of 9.44 g of finely-ground indazole in 80 ml of dry tertiary butyl alcohol was added .36 g of acrylonitrile and then 4 ml of a freshly-prepared alcoholic solution of trimethylphenylammonium ethoxide. The reaction mixture was left at 40-43° for 3 days. First the indazole dissolved and then a precipitate formed, which was filtered out and washed with a little tertiary butyl alcohol and water. There was obtained 10.24 g of a colorless substance with m. p. 83.5-84.5°; another 1.52 g of this compound, m. p. 83-84°, was obtained from the mother liquor. Total yield 86%. After recrystallization from aqueous alcohol, β-(indazyl-1)-propionitrile had m. p. 85° (literature data: 84-85°); colorless prisms, readily soluble in chloroform, acetone, ethyl acetate, and dichloroethane, and less soluble in alcohol, benzene, and ether.

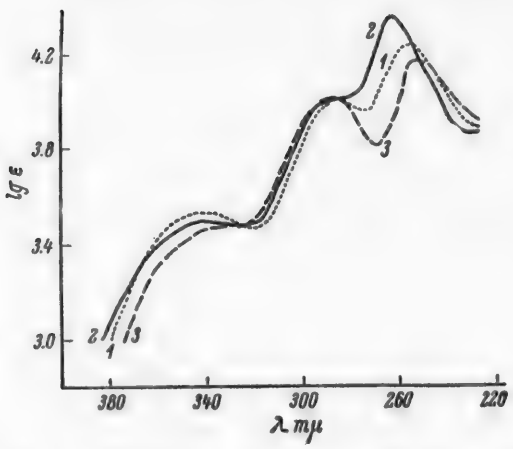


Fig. 5. Ultraviolet spectra. 1) 1-Methyl-6-nitroindazole; 2) 2-methyl-6-nitroindazole; 3) 6-nitroindazole.

β-(Indazyl-1)-propiothioamide. Into a solution of 1.71 g of β-(indazyl-1)-propionitrile in 60 ml of saturated alcoholic ammonia solution at room temperature, a current of dry hydrogen sulfide was passed for 3.5 hours. The reaction mixture was left in a closed flask at room temperature for 3 days; the mixture was then evaporated in vacuo to a volume of about 50 ml, 15 ml of cold water added to the residue, and the resulting precipitate filtered out, washed with water, and dried. There was obtained 1.6 g of a substance with m. p. 140-141° (from 50% alcohol); colorless prisms, very soluble in acetone, hot alcohol, and dioxane, less soluble in ethyl acetate, alcohol, and benzene, and nearly insoluble in ether and chloroform.

Found %: C 58.40; H 5.21; N 20.39; S 15.41. $C_{10}H_{11}N_3S$. Calculated %: C 58.51; H 5.40, N 20.47; S 15.62.

β-(3-Chloroindazyl-1)-propionitrile was prepared by the method described above from equimolar quantities of 3-chloroindazole and acrylonitrile in 91.3% yield. Colorless prisms with m. p. 80-81° (from 50% aqueous alcohol), readily soluble in acetone, chloroform, ether, benzene, ethyl acetate, and alcohol, and nearly insoluble in petroleum ether and water.

Found %: C 58.72; H 4.08; N 20.09; Cl 17.44. $C_{10}H_8N_3Cl$. Calculated %: C 58.40; H 3.92; N 20.43; Cl 17.24.

β-(3-Chloroindazyl-1)-propiothioamide. Into a solution of 4.1 g of β-(3-chloroindazyl-1)-propionitrile in 60 ml of saturated alcoholic ammonia solution (at room temperature), a current of dry hydrogen sulfide was passed for 1.5 hours. Then the reaction mass was left for 2 days. The resulting precipitate was filtered out, washed with water, and dried. There was obtained 4.41 g (92.1%) of a substance with m. p. 168° (from alcohol), very soluble in acetone, dioxane, and ethyl acetate, less soluble in alcohol, and slightly soluble in benzene, ether, and chloroform.

Found %: C 49.96; H 4.20; N 17.30; S 13.63; Cl 15.02. $C_{10}H_{10}N_3SCl$. Calculated %: C 50.10; H 4.20; N 17.53; S 13.38; Cl 14.79.

β-(6-Aminoindazyl-1)-propionitrile. a) 6-Aminoindazole was cyanoethylated, as in the preparation of β-indazyl-1-propionitrile. Colorless tablets with a rosy tint, having m. p. 126-127° (from water), readily soluble in dioxane, acetone, ethyl acetate, chloroform, and hot water, less soluble in alcohol, and slightly soluble in benzene and ether.

Found %: C 64.69; H 5.41; N 29.98. $C_{10}H_{10}N_4$. Calculated %: C 64.49; H 5.41; N 30.09.

b) Into a solution of 0.65 g of β-(6-nitroindazyl-1)-propionitrile in 24 ml of dry pyridine and 0.33 g of triethylamine, a current of dry hydrogen sulfide was passed for 1.5 hours. In this case, the yellow solution gradually became greenish, then dark. At the end of the reaction, the pyridine was removed in vacuo, and the residue was ground with 15 ml of water, filtered out, and dried. There was obtained 0.63 g of a light-brown substance with m. p. 114-117°. On solution of the latter in 25 ml of 50% alcohol, 0.2 g of sulfur remained. After removal of the sulfur and purification with charcoal, 0.38 g of a pale, rose-colored substance with m. p. 124° was obtained from the solution. After recrystallization from water the substance had m. p. 126-127°, did not contain sulfur, and did not give any melting-point depression with β-(6-aminoindazyl-1)-propionitrile prepared by method "a."

β-(6-Aminoindazyl-1)-propiothioamide was prepared similarly to β-indazyl-1-propiothioamide. Pellets with a pale-rose tint, having m. p. 156-157° (from water), very soluble in acetone, dioxane, and hot water, less soluble in ethyl acetate and alcohol, and insoluble in ether, chloroform, and benzene.

Found %: C 54.40; H 5.34; N 25.32; S 14.81. $C_{10}H_{12}N_4S$. Calculated %: C 54.52; H 5.49; N 25.43; S 14.56.

β-(6-Nitroindazyl-1)-propionitrile was prepared by the cyanoethylation of 6-nitroindazole with an excess of acrylonitrile (50%), by the method described above, in 96.2% yield. Yellow prisms with m. p. 191-192° (from alcohol), very soluble in acetone, dioxane, and ethyl acetate and less soluble in alcohol, benzene, and ether.

Found %: C 55.33; H 3.70; N 25.88. Calculated %: C 55.55; H 3.73; N 25.92.

SUMMARY

Indazyl-2-acetothioamide and β-(indazyl-1)-, β-(6-nitroindazyl-1)-, β-(6-aminoindazyl-1)-, and β-(3-chloroindazyl-1)-propiothioamides were synthesized.

It was shown that the cyanoethylation of indazole, as well as 6-nitro-6-amino-, and 3-chloroindazoles, takes place in position 1.

It was confirmed by investigations of the ultraviolet spectra of indazole, 3-chloroindazole, and 6-nitroindazole, that these compounds have a benzoid structure.

LITERATURE CITED

[1] T. S. Gardner, E. Wenis, and J. Lee, J. Org. Ch. 19, 753 (1954).

[2] D. Libermann, N. Rist, and F. Grumbach, Bull. Soc. Chim. Biol. 38, 231 (1956).

[3] D. Libermann, N. Rist, F. Grumbach, and S. Cals, Bull. Soc. Chim. Biol. 39, 1195 (1957).

[4] F. P. Doyle, W. Ferrier, et al., J. Chem. Soc. 2853 (1956).

[5] K. v. Auwers and H. G. Allardt, Ber. 59, 95 (1926).

[6] C. Ainworth, J. Am. Chem. Soc. 80, 965 (1958).

[7] A. P. Terent'ev and A. N. Kost, Reactions and Methods of Investigation of Organic Compounds, II [in Russian] (Goskhimizdat, 1952) p. 121.

[8] A. P. Terent'ev, A. N. Kost, and V. M. Potapov, Zhur. Obshchei Khim. 18, 82 (1948); R. C. Elderfield, W. J. Gensler, et al., J. Am. Chem. Soc. 68, 1259 (1946).

[9] V. Rousseau and H. G. Lindwall, J. Am. Chem. Soc. 72, 3047 (1950).

CERTAIN SUBSTITUTED LILOLIDENES

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3977-3982,

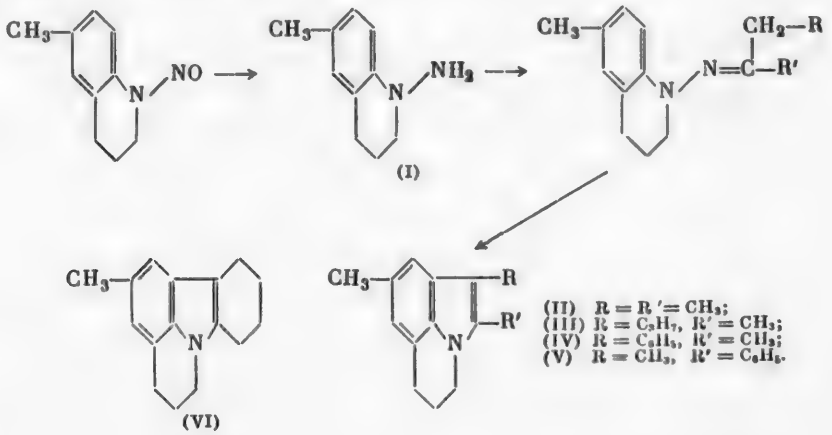
December, 1959

Original article submitted November 26, 1958

In the preceding articles, a synthesis of lilolidenes [1] and benzopyrrolizidenes [2], based on the Fischer reaction with 1-aminotetrahydroquinoline or 1-aminoindolines, respectively, was described. The tri- and tetracyclic structures formed in this case have a nitrogen atom in the junction position and are similar to the nuclear structures of lycorine-type alkaloids.

In the present work, in order to develop the method, we synthesized certain substituted lilolidenes, including some having a carboxyl or hydroxyl group. On synthesis of 1-nitroso-1, 2, 3, 4-tetrahydroquinoline by a method described earlier [1], we obtained this substance in the crystalline state. Similarly, nitrosation of 6-methyl-1, 2, 3,4-tetrahydroquinoline gave the corresponding nitroso compound, which was reduced to 1-amino-6-methyl-1,2, 3,4-tetrahydroquinoline (I).

On treatment with 20% sulfuric acid of the hydrazones formed in the reactions of 1-amino-6-methyl-1,2,3, 4-tetrahydroquinoline (I) with methyl ethyl ketone, methyl butyl ketone, phenylacetone[methyl benzyl ketone], cyclohexanone, and propiophenone, we obtained the corresponding 2-methyllilolidenes (II)-(VI), having alkyl or aryl substituents in positions 9 and 10. Comparison of the ultraviolet absorption spectra with those described earlier [1] shows that the methyl group in position 2, as was to be expected, has no effect on the absorption maximum. The spectra of compounds (II), (III), and (VI) are practically identical (see Fig. 1). The presence of a phenyl group in position 9, i.e., in the case of 9-phenyllilolidene-9 (V), causes a pronounced bathochromic shift of the absorption maximum from 292-295 to 304 mμ, and on introduction of a phenyl group in position 10, i.e., in the case of 2,9-dimethyl-10-phenyllilolidene-9 (IV), the opposite effect, a hypsochromic shift of the absorption maximum (λ_{max} 280 mμ), is observed.



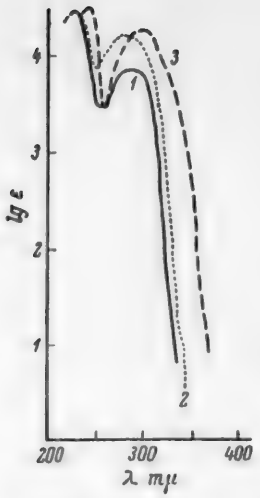
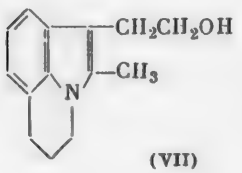


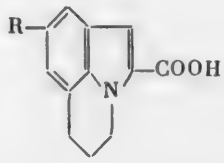
Fig. 1. UV absorption spectra of 2-methyllilolidenes-9 (in methanol). 1) 2,9,10-Trimethyllilolidene-9 (II); 2) 2,9-dimethyl-10-phenyllilolidene-9 (IV); 3) 2,10-dimethyl-9-phenyllilolidene-9 (V).

In order to synthesize lilolidenic compounds having functional groups, we brought acetopropyl alcohol [1-hydroxypentanone-4] into reaction with 1-amino-1,2,3,4-tetrahydroquinoline and obtained the tricyclic analog of tryptophol (VII) in 89% yield.

Using a somewhat modified Barger method [3], we prepared lilolidene-9-carboxylic acid (VIII) in 52% yield; its sodium and potassium salts were very soluble in water. In the case of 1-amino-6-methyl-1, 2,3,4-tetrahydroquinoline, this reaction (with pyruvic acid) goes even more smoothly and gives 2-methyllilolidene-9-carboxylic acid (IX) in approximately 90% yield.

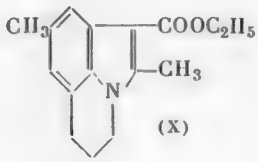


(VII)



(VIII) R = H,
(IX) R = CH3.

Similarly, proceeding from acetoacetic ester, we synthesized 2,9-dimethyl-10-carbethoxyllilolidene-9 (X). It is interesting to note that a carboxyl group in position 9 in compound (IX) causes an even greater displacement of the light-absorption maximum than the phenyl radical. As regards substance (X) with a carbethoxy group in position 10, the absorption maximum in this case was scarcely shifted (292 mμ); however, there was a second maximum in the 240 mμ region, which also was vaguely discernible in the case of alkyllilolidenes (see Fig. 2).



(X)

In attempts at the direct synthesis of 9-alkyllilolidenes by rearrangement of the hydrazones formed by 1-amino-1,2,3,4-tetrahydroquinoline or its 6-methyl analog (I) with various aldehydes, we observed severe tarring or recovered the starting materials. The hydrazones of propion-, butyr-, and isovaleraldehydes were used in this way, sulfuric acid, zinc chloride, cuprous chloride, alcoholic hydrogen chloride, and polyphosphoric acid being employed as condensing agents. Difficulties of this kind in the Fischer reaction were noted earlier in the case of 1-aminoindolines [2].

EXPERIMENTAL

1-Nitroso-1,2,3,4-tetrahydroquinoline. To a cooled solution of 53.2 g of 1,2,3,4-tetrahydroquinoline in 400 ml of 15% sulfuric acid, a saturated aqueous solution of 34 g of sodium nitrite was cautiously added dropwise at 0°. The precipitated crystals were thoroughly washed with water and dried for several hours in air. There was obtained 59 g (92%) of a substance with m. p. 20-22°. After recrystallization from ether, m. p. 22°. The substance was unstable on keeping (it turned red and softened).

Found %: N 17.19, 17.24. $C_9H_{10}ON_2$. Calculated %: N 17.28.

1-Nitroso-6-methyl-1,2,3,4-tetrahydroquinoline. 1-Formyl-6-methyl-1,2,3,4-tetrahydroquinoline was obtained in 90% yield through reduction of 71.5 g of 6-methylquinoline (by boiling for 20 hours with 138 g of anhydrous formic acid and 101 g of triethylamine) by a method described earlier [4]. When the product was boiled

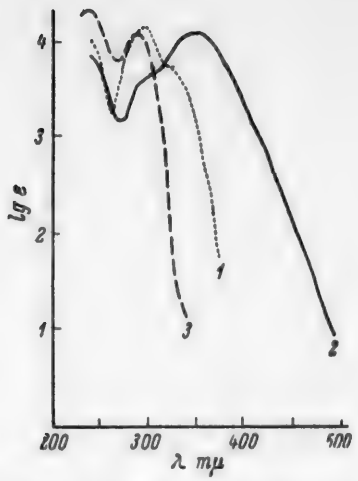


Fig. 2. UV absorption spectra of lilolidenecarboxylic acids (in chloroform). 1) 2-Methyl-9-carboxylilolidene-9 (IX); 2) original hydrazone of 1-amino-6-methyltetrahydroquinoline with pyruvic acid (XI); 3) 2,9-dimethyl-10-carbethoxylilolidene-9

for 1 hour with three times its volume of concentrated hydrochloric acid, 6-methyl-1,2,3,4-tetrahydroquinoline was obtained in 94.5% yield. After redistillation, b. p. 116-117° (8 mm), m. p. 37° [4].

On nitrosation of 74 g of this substance by treatment with 41 g of sodium nitrite in sulfuric acid as described above, 57.5 g (65%) of 1-nitroso-6-methyl-1,2,3,4-tetrahydroquinoline, m. p. 64° [5], was obtained.

1-Amino-6-methyl-1,2,3,4-tetrahydroquinoline (I). On reduction of 52.8 g of 1-nitroso-6-methyl-1,2,3,4-tetrahydroquinoline by the method described for the synthesis of 1-amino-1,2,3,4-tetrahydroquinoline [1], 29.2 g (60%) of 1-amino-6-methyl-1,2,3,4-tetrahydroquinoline, b. p. 110-120° (3 mm), was obtained. The substance crystallized on standing. After recrystallization from petroleum ether, m. p. 38°.

Found %: N 17.34, 17.41. $C_{10}H_{14}N_2$. Calculated %: N 17.27.

2,9,10-Trimethyllilolidene-9 (II). A mixture of 3.25 g of 1-amino-6-methyl-1,2,3,4-tetrahydroquinoline (I) and 2.9 g of methyl ethyl ketone was refluxed for 1 hour in a water bath. The unreacted ketone was driven off in vacuo, 10 ml of 20% sulfuric acid was added to the mixture, and the latter was shaken and heated for 30 minutes in a water bath. The oil which separated on cooling gradually crystallized. Yield 3.0 g (75%). After three recrystallations from methanol, m. p. 73°.

λ max. 294 mμ, lg ε 3.84 (in methanol).

Found %: C 84.28, 84.16; H 8.82, 8.74. $C_{14}H_{17}N$. Calculated %: C 84.36; H 8.69

Picrate – m.p. 155–156° (from alcohol).

Found %: C 55.93, 56.15; H 4.81, 4.83. $C_{20}H_{20}O_7N_4$. Calculated %: C 55.91; H 4.68.

2,9-Dimethyl-10-propyllilolidene-9 (III). Similarly to the preceding, from 3.25 g of 1-amino-6-methyltetrahydroquinoline (I) and 4 g of methyl butyl ketone, 2.7 g (57%) of lilolidene (III) was obtained. M. p. 67° (from methanol).

λ max. 292 mμ, log ε 3.83 (in methanol).

Found %: C 84.74, 84.79; H 9.44, 9.43. $C_{16}H_{21}N$. Calculated %: C 84.53; H 9.31.

Picrate – m. p. 120° (decomp.) (from alcohol).

Found %: C 57.73, 57.89; H 5.33, 5.48. $C_{22}H_{24}O_7N_4$. Calculated %: C 57.89; H 5.27.

2,9-Dimethyl-10-phenyllilolidene-9 (IV). Similarly, from 3.25 g of 1-amino-6-methyltetrahydroquinoline (I) and 2.7 g of phenylacetone [methyl benzyl ketone], 4.0 g (77%) of lilolidene (IV) was obtained. M. p. 116° (from methanol).

λ max. 280 mμ, log ε 4.20 (in methanol).

Found %: C 87.19, 87.28; H 7.44, 7.40. $C_{19}H_{19}N$. Calculated %: C 87.31; H 7.33.

2,10-Dimethyl-9-phenyllilolidene-9 (V). From 3.25 g of 1-amino-6-methyltetrahydroquinoline (I) and 2.7 g of propiophenone under the same conditions as in the preceding experiment, 0.5 g (10%) of dimethylphenyllilolidene (V) was obtained. M. p. 108° (from methanol).

λ max. 304 mμ, log ε 4.25 (in methanol).

Found %: C 87.13, 87.22; H 7.25, 7.37. $C_{19}H_{19}N$. Calculated %: C 87.31; H 7.33.

Picrate – m. p. 129.5° (from alcohol).

Found %: C 61.13, 61.14; H 4.68, 4.78. $C_{25}H_{22}O_7N_4$. Calculated %: C 61.23; H 4.87.

2,9-Dimethyl-10-carbethoxylilolidene-9 (X). Similarly, from 3.25 g of 1-amino-6-methyltetrahydroquinoline (I) and 2.6 g of acetoacetic ester, 3.5 g (68%) of ester (X) was obtained. M. p. 118° (from methanol).

λ max. 240, 292 mμ, log ε 4.31, 4.08 (in methanol).

Found %: C 74.54, 74.61; H 7.42, 7.47. $C_{16}H_{19}O_2N$. Calculated %: C 74.69; H 7.45.

Picrate—m. p. 142° (from alcohol).

Found %: N 11.71, 11.86. $C_{22}H_{22}O_9N_4$. Calculated %: N 11.52.

9-Methyl-10-(2-hydroxyethyl)lilolidene-9 (VII). Similarly, from 1.2 g of 1-amino-1,2,3,4-tetrahydroquinoline and 1.0 g of acetopropyl alcohol [1-hydroxypentanone-4] in the presence of 5 ml of 20% sulfuric acid, 1.55 g (89%) of the analog of tryptophol (VII) was obtained. M. p. 89° (from 50% alcohol).

λ max. 290 mμ, log ε 3.83 (in methanol).

Found %: C 77.96, 78.06; H 8.04, 7.98. $C_{14}H_{17}ON$. Calculated %: C 78.11; H 7.95.

9-Carboxylilolidene-9 (VIII). To a solution of 3.0 g of 1-amino-1,2,3,4-tetrahydroquinoline in 30 ml of 25% acetic acid, 2.64 g of pyruvic acid was added; the precipitated crystals of the hydrazone were filtered out and washed with water. Yield 3.9 g (94%); after recrystallization from a benzene-petroleum ether mixture (2:1) the substance had m. p. 99° [3]. The hydrazone obtained was heated for 1 hour at 60° with 50 ml of 10% hydrochloric acid. The resulting precipitate was filtered out, washed with water, and twice recrystallized from benzene. Yield 1.98 g (53%); m. p. 212° [3].

2-Methyl-9-carboxylilolidene-9 (IX). From 3.25 g of 1-amino-6-methyl-1,2,3,4-tetrahydroquinoline (I) and 2.64 g of pyruvic acid in a similar experiment, 4.6 g (99%) of the corresponding hydrazone (XI) was obtained; m. p. 107° [from a benzene-petroleum ether mixture (2:1)].

λ max. 365 mμ, log ε 4.07 (in chloroform).

Found %: N 12.22, 12.32. $C_{13}H_{16}O_2N_2$. Calculated %: N 12.16.

The hydrazone obtained was heated for 1 hour at 60° with 50 ml of 10% hydrochloric acid, and 4.0 g (92%) of 2-methyl-9-carboxylilolidene-9 (IX) was isolated. After five recrystallizations from benzene, m. p. 227-228°.

λ max. 301 mμ, log ε 4.16 (in chloroform).

Found %: C 71.93, 72.21; H 5.84, 5.90. $C_{13}H_{13}O_2N$. Calculated %: C 72.53; H 6.09.

12-Methyl-1,2,3,4,6,7,8,9-octahydropyrido-*l*,m-1,2,3-carbazole (VI). A mixture of 0.88 g of 1-amino-6-methyl-1,2,3,4-tetrahydroquinoline (I) and 0.8 g of cyclohexanone was heated in a water bath for 45 minutes, 5 ml of 20% sulfuric acid was added, and the mixture was shaken and heated for 30 minutes in the water bath. On cooling, 1.1 g (90%) of octahydropyridocarbazole (VI) was obtained. After three recrystallizations from methanol, m. p. 88°.

λ max. 292 mμ, log ε 3.92 (in methanol).

Found %: C 84.94, 85.13; H 8.67, 8.71. $C_{16}H_{19}N$. Calculated %: C 85.27; H 8.57.

Picrate—m. p. 158-158.5° (from alcohol).

Found %: N 12.51, 12.58. $C_{22}H_{22}O_7N_4$. Calculated %: N 12.33

SUMMARY

The synthesis of a number of tri- and tetracyclic structures of the lilolidene type, containing alkyl and aryl radicals and certain functional groups, is described.

LITERATURE CITED

[1] A. N. Kost and L. G. Yudin, Khim. Nauka i Prom. 2, 800 (1957); A. N. Kost, L. G. Yudin, and A. N. Terent'ev, Zhur. Obshchei Khim. 29, 1949 (1959).•

[2] A. N. Kost, L. G. Yudin, Yu. A. Berlin, and A. P. Terent'ev, Zhur. Obshchei Khim. 29, 3834 (1959).•

[3] G. Barger and E. Dayer, J. Am. Chem. Soc. 60, 2414 (1938).

[4] L. G. Yudin, A. N. Kost, E. Kh. Zolotarev, and A. N. Mirza, Vestnik Moskov. Gosudarst. Univ., Ser. Khim. 2, 169 (1958).

[5] E. Bamberger and P. Wulz, Ber. 24, 2055 (1891).

•Original Russian pagination. See C. B. translation.

FUNCTIONAL DERIVATIVES OF MALONDIALDEHYDE AND THEIR REACTIONS•

IX. 1,3-DICHLORO-1,3-DIALKOXYPROPANES. A NEW METHOD OF PREPARING CHLORO- AND BROMOMALONDIALDEHYDES

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3982-3987,

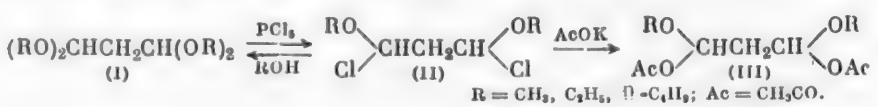
December, 1959

Original article submitted December 7, 1958

In the preceding articles we showed that the full acetals of malondialdehyde (I), which are now available [1b], are convenient starting materials for the synthesis of a number of the simplest heterocyclic compounds [1c]. It was of interest to find methods of passing over from the acetals (I) to derivatives of malondialdehyde substituted in the methylene group—primarily chloro- and bromomalondialdehydes. Until now the latter have been synthesized through the α, β-dihalo-β-formylacrylic acids [2,3] or by the halogenation of β-ethoxyacrolein diethyl acetal [3] or an acetal of propiolaldehyde [4]; chloromalondialdehyde was prepared also by the hydrolysis of 1,1,2,3-tetrachloropropene-2 with concentrated sulfuric acid [5].

We found that treatment of acetals (I) with bromine in pyridine or N-bromosuccinimide in carbon tetrachloride leads to a mixture of bromination products, from which the individual substances could not be isolated. Besides, cases of successful bromination of the simplest α-chloroethyl alkyl ethers $CH_3CH(OR)Cl$, leading to the formation of α, β-dibromoethyl alkyl ethers $CH_2BrCH(OR)Br$, are described in the literature [6]. Proceeding from this, we attempted to synthesize the hitherto-unknown 1,3-dichloro-1,3-dialkoxypropanes (II) (having the structure of di-α-chloro ethers), whose halogenation might lead to the formation of derivatives of chloro- and bromomalondialdehyde.

We prepared 1,3-dichloro-1,3-dialkoxypropanes (II, R = CH_3, C_2H_5, n-C_4H_9) through the reactions of 1,1,3,3-tetraalkoxypropanes (I) with phosphorus pentachloride or thionyl chloride. In the case of the tetramethyl acetal (I, R = CH_3), the reaction with phosphorus pentachloride went very vigorously, and it was expedient to carry it out in a phosphoryl chloride medium; as the weight of the alkyl groups increased, the vigor of the reaction diminished. After driving off the phosphoryl chloride, di-α-chloro ethers (II, R = CH_3 and C_2H_5) were isolated by distillation in vacuo; in this case some decomposition occurred. For this reason the higher-boiling one (II, R = = n-C_4H_9) could not be isolated in an analytically pure state, and it was converted without distillation to the 1,3-diacetoxy-1,3-di-n-butoxy derivative (III, R = n-C_4H_9).



R = CH_3, C_2H_5, n-C_4H_9; Ac = CH_3CO.

Di-α-chloro ethers (II) are unstable, colorless, fuming liquids with a sharp odor, rapidly hydrolyzed by water with the formation of solutions containing free malondialdehyde. Both halogen atoms in these compounds are easily hydrolyzed and may be titrated quantitatively by the mercurometric method; on treatment with potassium

• We decided to combine our works on the subject into a series beginning with this article. For the preceding articles of this series see [1].

acetate in glacial acetic acid solution they are smoothly replaced by acetoxy groups with the formation of 1,3-dialkoxy-1,3-diacetoxypropanes (III). Treatment of di-α-chloro ether (II, R = C_2H_5) with alcohol leads back to 1,1,3,3-tetraethoxypropane.

The high mobility of the halogen atoms sharply distinguishes di-α-chloro ethers (II) from isomeric, unsymmetrical 1,1-dichloro-3,3-dialkoxypropanes—acetals of β,β-dihalopropionaldehydes [1f], the possibility of whose formation in the reaction of phosphorus pentachloride with acetals (I) could not be excluded. The symmetrical structure of di-α-chloro ethers (II) and the presence of two asymmetric carbon atoms make possible the formation of a mixture of the meso-form and the racemate in the reaction. However, we have not yet succeeded in resolving the substances obtained into isomeric compounds; investigations in this direction are in progress.

When 1 mole of 1,1,3,3-tetraethoxypropane was heated with 3 moles of phosphorus pentachloride, 1,2,3-trichloro-1,3-diethoxypropane was obtained in 32% yield; the structure of the latter was proved by its hydrolysis to chloromalondialdehyde; under these conditions the chlorinating action of phosphorus pentachloride is manifested.

$$\underset{(I)}{(C_2H_5O)_2CHCH_2CH(OC_2H_5)_2} + 3PCl_5 \longrightarrow$$

$$\longrightarrow \begin{matrix} C_2H_5O \\ Cl \end{matrix}\!\!>\!CHCHClCH<\!\!\begin{matrix} OC_2H_5 \\ Cl \end{matrix} + 2C_2H_5Cl + 2POCl_3 + PCl_3 + HCl$$

As we expected, the di-α-chloro ethers (II) prepared by us (shown in reaction II, R = C_2H_5) are easily chlorinated by sulfuryl chloride in the presence of benzoyl peroxide or brominated by bromine on illumination, the corresponding 1,2,3-trihalo-1,3-dialkoxypropanes (IV, X = Cl or Br) being formed. For halogenations it is expedient to use undistilled di-α-chloro ether (II); distillation losses are thus avoided.

$$\begin{matrix} C_2H_5O \\ Cl \end{matrix}\!\!>\!CHCH_2CH<\!\!\begin{matrix} OC_2H_5 \\ Cl \end{matrix} \underset{(II)}{} \xrightarrow[\text{or } Br_2]{SO_2Cl_2}$$

$$\longrightarrow \begin{matrix} C_2H_5O \\ X \end{matrix}\!\!>\!CHCHXCH<\!\!\begin{matrix} OC_2H_5 \\ Cl \end{matrix} \underset{(IV)}{}$$

$$\xrightarrow{H_2O} O{=}CHCHXCH{=}O \quad (V)$$

$$\xrightarrow{C_2H_5OH} (C_2H_5O)_2CHCHXCH(OC_2H_5)_2 \quad (VI)$$

1,2,3-Trihalo-1,3-diethoxypropanes (IV) also are unstable compounds which are decomposed to a considerable degree on distillation; hence we hydrolyzed them with water without purification and, after neutralization of the excess acid, extracted dialdehyde (V, X = Cl or Br) from the aqueous solution with ether; yields 47 and 56%, respectively, reckoned on 1,1,3,3-tetraethoxypropane. To obtain tetraacetals (VI), the reaction mass after halogenation was treated with anhydrous alcohol, neutralized, and fractionated in vacuo; yields of acetals (VI, X = Cl or Br) were 46 and 71% respectively, reckoned on 1,1,3,3-tetraethoxypropane.

The results obtained indicate that 1,1,3,3-tetraalkoxypropanes may be used successfully for the synthesis of halomalondialdehydes and their derivatives.

EXPERIMENTAL

1,3-Dichloro-1,3-dimethoxypropane. To a mixture of 41.7 g of phosphorus pentachloride and 15 ml of phosphoryl chloride, 16.5 g of 1,1,3,3-tetramethoxypropane was gradually added, the mixture being cooled with ice and stirred; then the mixture was further stirred for 0.5 hour at room temperature. The phosphoryl chloride was driven off at 30 mm in a water bath whose temperature did not exceed 45-50°, and the residue was fractionated in vacuo. There was obtained 13.1 g (75%) of 1,3-dichloro-1,3-dimethoxypropane.

B.p. 44-48° (4.5 mm), n_D^{20} 1.4460, d_4^{20} 1.2182, MR_D 37.91; Calc. 38.30.

Found %: $Cl_{ion.}$ 41.08, 41.04. $C_5H_{10}O_2Cl_2$. Calculated %: $Cl_{ion.}$ 40.98.

The dichlorodimethoxypropane was a colorless liquid with a sharp odor, fuming in air, which rapidly turned yellow on keeping; in the cold with access of moisture, it was kept unchanged for several days. Insoluble in water, but rapidly hydrolyzed by it with the formation of solutions which readily decolorized bromine and gave a red-violet color with ferric chloride solution, which is characteristic of aqueous malondialdehyde solutions.

1,3-Dimethoxy-1,3-diacetoxypropane. To a well stirred and cooled mixture of 15 g of anhydrous potassium acetate and 45 ml of glacial acetic acid, 13 g of 1,3-dichloro-1,3-dimethoxypropane was gradually added; potassium chloride began to separate almost immediately. The mixture was stirred for 2.5 hours at 12-15°, the precipitate filtered out and washed with glacial acetic acid, and the filtrate fractionated in vacuo. The acetic acid was distilled off at 45-50 mm, after which 9.5 g (58%) of the substance was collected.

B.p. 81-84° (1 mm), n_D^{20} 1.4198, d_4^{20} 1.1072, MR_D 50.26; Calc. 50.30.
Found %: C 48.91, 48.88; H 7.48, 7.40. $C_9H_{16}O_6$. Calculated %: C 49.09; H 7.32.

A colorless liquid, insoluble in water; on brief heating with water it went into solution as a result of hydrolysis. Soluble in common organic solvents.

1,3-Dichloro-1,3-diethoxypropane. a) With phosphorus pentachloride. To 43.7 g of phosphorus pentachloride, 22 g of 1,1,3,3-tetraethoxypropane was slowly added with cooling. After a liquid phase appeared in the reaction mixture and the vigor of the reaction diminished, cooling was stopped and addition continued at room temperature; the mixture was stirred for 1 hour more, until the phosphorus pentachloride was entirely gone. The phosphoryl chloride was driven off in vacuo at a bath temperature not over 50°, and the residue was fractionated. There was obtained 17.0 g (84%) of 1,3-dichloro-1,3-diethoxypropane.

B.p. 58-63.5° (1-1.5 mm), n_D^{20} 1.4435, d_4^{20} 1.1242, MR_D 47.48; Calc. 47.55.

Found %: Cl_{ion} 35.28, 35.57. Calculated %: Cl_{ion} 35.32.

b) With thionyl chloride. A mixture of 22 g of 1,1,3,3-tetraethoxypropane, 30 ml of dry carbon tetrachloride, two drops of pyridine, and 26.4 g of freshly-distilled thionyl chloride, carefully protected from atmospheric moisture, was cautiously heated in a water bath, the temperature of the latter being gradually raised to 65-70°. After 7-8 hours the evolution of gaseous reaction products had practically ceased. The excess thionyl chloride and solvent were removed in vacuo (110-120 mm), and the residue was fractionated. There was obtained 15.6 g (77%) of 1,3-dichloro-1,3-diethoxypropane, b. p. 58-62.5° (1.5 mm), n_D^{20} 1.4438.

1,3-Diethoxy-1,3-diacetoxypropane. From 4.0 g of 1,3-dichloro-1,3-diethoxypropane, 4.0 g of potassium acetate, and 10 ml of acetic acid, under the conditions given in the description of the corresponding methoxy derivative, 2.1 g (43%) of 1,3-diethoxy-1,3-diacetoxypropane was obtained after two distillations.

B.p. 99-102° (2.5 mm), n_D^{20} 1.4200, d_4^{20} 1.0488, MR_D 59.76; Calc. 59.60.

Found %: C 53.65, 53.69; H 8.40, 8.36. $C_{11}H_{20}O_6$. Calculated %: 53.25; H 8.12.

Reaction of 1,3-dichloro-1,3-diethoxypropane with alcohol. A mixture of 5 g of 1,3-dichloro-1,3-diethoxypropane and 25 ml of anhydrous alcohol was left at room temperature for 24 hours, after which it was poured into saturated sodium bicarbonate solution, and the substance which separated was extracted with ether. The etheral extracts were dried with anhydrous sodium sulfate. The ether was evaporated. After distillation of the residue in vacuo, 4.27 g of 1,1,3,3-tetraethoxypropane was obtained.

B.p. 83.5-87° (6 mm), n_D^{20} 1.4112.

According to literature data [1b]: b.p. 86-87° (6 mm), n_D^{20} 1.4105.

1,3-Dichloro-1,3-dibutoxypropane; 1,3-dibutoxy-1,3-diacetoxypropane. To 20.8 g of phosphorus pentachloride, 16.0 g of 1,1,3,3-tetra-n-butoxypropane was added with stirring. The reaction was accompanied by only slight spontaneous warming. The reaction mixture was treated as in the preceding experiments. After driving off the phosphoryl chloride, the remaining 1,3-dichloro-1,3-dibutoxypropane (11.2 g), without purification (it decomposed to a considerable degree on distillation in vacuo), was converted to the corresponding diacetate; for this it was gradually added to 12 g of anhydrous potassium acetate in 35 ml of glacial acetic acid. After the usual treatment of the reaction mixture the substance obtained was twice fractionated in vacuo.

Yield of 1,3-dibutoxy-1,3-diacetoxypropane, 4.9 g.

B.p. 158-162° (1-1.5 mm), n_D^{20} 1.4290, d_4^{20} 1.0003, MR_D 78.32; Calc. 78.09.

Found %: C 59.85, 59.76; H 9.42, 9.64. $C_{15}H_{28}O_6$. Calculated %: C 59.20; H 9.26.

1,2,3-Trichloro-1,3-diethoxypropane. To a suspension of 33.4 g of phosphorus pentachloride in 25 ml of dry carbon tetrachloride, 11 g of 1,1,3,3-tetraethoxypropane was rapidly added, the mixture being boiled continuously; the mixture was then refluxed for 1.5 hours, the solvent and phosphoryl chloride driven off in vacuo, and the residue twice fractionated. There was obtained 3.8 g (32%) of 1,2,3-trichloro-1,3-diethoxypropane.

B.p. 83-85° (1 mm), n_D^{20} 1.4695, d_4^{20} 1.2432, MR_D 52.75; Calc. 52.40.

Found %: Cl_{total} 44.93, 45.19; $Cl_{ion.}$ 30.12, 29.95. $C_7H_{13}O_2Cl_3$. Calculated %: Cl_{total} 45.21; $Cl_{ion.}$ 30.14.

One g of 1,2,3-trichloro-1,3-diethoxypropane was shaken with 20 ml of water until the substance was completely dissolved, after which the solution was extracted several times with ether and the extracts dried. After evaporation of the ether the residue completely crystallized. After sublimation of the crystals in vacuo there was obtained 0.25 g of chloromalondialdehyde, m. p. 142.5-144°, which gave no melting point depression with the substance prepared by chlorination of β-ethoxyacrolein diethyl acetal [3].

Chloromalondialdehyde. To the undistilled 1,3-dichloro-1,3-diethoxypropane obtained from 87.4 g of phosphorus pentachloride and 44 g of 1,1,3,3-tetraethoxypropane after distilling off the phosphoryl chloride in vacuo, a trace of benzoyl peroxide was added, after which 28.4 g of freshly-distilled sulfuryl chloride was gradually added at 40-50°; the mixture was heated until the evolution of gaseous substances ceased, the bath temperature being raised gradually to 60-65°. The reaction mass obtained (45.5 g) was divided into two equal parts. The first half was shaken with 160 ml of 5% soda solution until the mixture became homogeneous. The unhydrolyzed residue (less than 1 ml) was drawn off and the water layer extracted with ether in a continuous-action extractor. The ethereal extracts were dried with sodium sulfate. The ether was removed and the residue dried in a vacuum desiccator and thoroughly washed with dry benzene. There was obtained 5.0 g (47%, reckoned on 1,1,3,3-tetraethoxypropane) of nearly colorless crystals with m. p. 139-140.5°. After sublimation in vacuo, chloromalondialdehyde had m. p. 144° and gave no melting-point depression in a mixture with the sample prepared above.

One hundred ml of anhydrous alcohol was added to the second half of the chlorination product and the mixture left at room temperature for 2 days, after which it was poured into sodium bicarbonate solution and extracted with ether. The ethereal extracts were dried with sodium sulfate, the ether removed, and the residue fractionated in vacuo. There was obtained 11.6 g (46%, reckoned on 1,1,3,3-tetraethoxypropane) of chloromalondialdehyde tetraethyl acetal.

B.p. 116-123° (12 mm), n_D^{20} 1.4340, d_4^{20} 1.0433. Literature data [7]: b.p. 116-120° (12 mm).

Bromomalondialdehyde. To the undistilled 1,3-dichloro-1,3-diethoxypropane obtained from 87.4 g of phosphorus pentachloride and 44 g of 1,1,3,3-tetraethoxypropane after driving off the phosphoryl chloride in vacuo, 9 ml of bromine was added dropwise with stirring and illumination. The resulting reaction mass (62.6 g) was divided into two equal parts. The first half was converted to bromomalondialdehyde by the method described above for preparing chloromalondialdehyde. The ether was removed and the residue treated with benzene; 5.8 g of nearly colorless crystals with m. p. 137-138.5° was obtained. An additional 2.85 g (57%) of the substance, m. p. 136-137°, was obtained by evaporation of the benzene mother liquors. After sublimation in vacuo, bromomalondialdehyde had m. p. 140-141° [8].

One hundred ml of anhydrous alcohol was added to the second half of the bromination product and the mixture left for 2 days, after which it was treated as in the preparation of the chloromalondialdehyde acetal. After double fractionation in vacuo, 21.4 g (71%) of bromoalondialdehyde tetraethyl acetal was obtained.

B.p. 140-143° (18.5 mm), n_D^{20} 1.4463, n_4^{20} 1.1902. Literature data [9]: b.p. 138-139° (18 mm).

SUMMARY

The 1,3-dichloro-1,3-dialkoxypropanes $Cl(RO)CHCH_2CH(OR)Cl$ (R = CH_3, C_2H_5, n-C_4H_9) were prepared through the interaction of the full acetals of malondialdehyde and phosphorus pentachloride or thionyl chloride, and cer-

tain of their reactions were investigated. Halogenation of these compounds leads to the formation of 1,2,3-trihalo-1,3-dialkoxypropanes, which may be hydrolyzed to chloro- or bromomalondialdehyde or converted to the corresponding acetals.

LITERATURE CITED

[1] T. V. Protopopova and A. P. Skoldinov: a) Zhur. Obshchei Khim. 26, 3355 (1956);* b) 27, 57 (1957);* c) 27, 1276 (1957);* d) 28, 240 (1958);* e) Khim. Nauka i Prom. 3 (4), 536 (1958). f) Zhur. Obshchei Khim. 28, 2428 (1958);* g) 28, 2805 (1958);* h) 29, 963 (1959).*

[2] H. Simonis, Ber. 32, 2084 (1899); 34, 509 (1901).

[3] W. Dieckmann and L. Platz, Ber. 37, 4643 (1904).

[4] J. Grard, C. r. 190, 187 (1930); Ann. Ch. (10), 13, 336 (1930).

[5] Germ. Pat. 261689; Zbl. II, 394 (1913).

[6] C. Swallen, and E. Boord, J. Am. Chem. Soc. 52, 654 (1930); M. N. Shchukina, Zhur. Obshchei Khim. 18, 1351 (1948).

[7] J. Cornforth, E. Fawaz, and L. Goldsworthy, J. Chem. Soc. 1549 (1949).

[8] R. Lespieau, C. r. 135, 538 (1901).

[9] S. Kofslein and R. Whiteley, J. Chem. Soc. 4012 (1953).

* Original Russian pagination. See C. B. translation.

INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

CX. POLAROGRAPHIC INVESTIGATION OF VINYLACETYLENIC HYDROCARBONS•

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3987-3992,

December, 1959

Original article submitted December 8, 1958

Among the chemical transformations of vinylacetylenic hydrocarbons studied in recent years in our laboratory, considerable attention has been directed to their catalytic hydrogenation. Experiments in this direction showed that hydrogen adds only to the acetylenic bond at first; in the case of vinylalkyl- and vinylarylacetylenes, however, the reaction goes much further, olefins or arylolefins being formed; the process goes much faster in the second stage than in the first. Therefore, vinylalkylacetylenes were reduced much faster than alkenyl- and isoalkenylacetylenes, while isopropenylacetylene was hydrogenated more rapidly than propenylacetylene. These differences in the character and rate of the hydrogenation of vinylacetylenic hydrocarbons of different structures were explained by their adsorption characteristics on palladium [1, 2].

It was of interest to compare data on the catalytic hydrogenation of vinylacetylenes with data on their reduction at the dropping mercury electrode. In our continued systematic study of the relation between the structure of vinylacetylenic hydrocarbons and their reactivity, therefore, we undertook the polarographic investigation of 12 vinylacetylenic hydrocarbons of different structures. In the literature there are some data on the polarography of unsaturated compounds with conjugated multiple bonds [3]; among the enyne compounds, however, only vinylacetylene has been investigated [4].

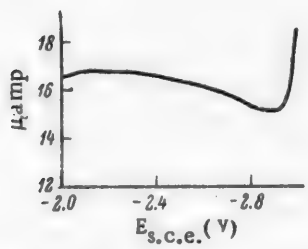

Fig. 1. Polarogram of oxygen wave in 75% dioxane (0.1 M solution of tetrabutylammonium iodide, 25 ± 0.1°).

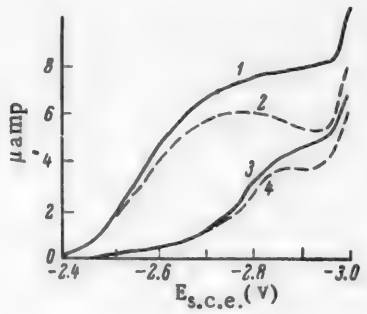

Fig. 2. Character of experimental (Curves 2 and 4) and corrected (Curves 1 and 3) polarograms of hydrocarbons I-VII (1 and 2) and VIII-XII (3 and 4).

• Enyne Compounds XXXIII.

In all cases investigated by us, extended waves were obtained; although the polarization curve was plotted in detail, we could not find more than one wave on the polarogram. Results of the measurements are given in Table 1.*

TABLE 1

Hydrocarbon	$E^{1}/_{2}$ (v)	(μ amp/mmole·liter)	c (mmoles/liter)
$CH{\equiv}C{-}CH{=}CH_2$ (I)	2.40	2.36	3.02
	2.40	3.11	4.87
$CH_3{-}C{\equiv}C{-}CH{=}CH_2$ (II)	2.63	6.67	0.76
	2.63	6.10	0.94
$C_2H_5{-}C{\equiv}C{-}CH{=}CH_2$ (III)	2.61	5.85	1.31
	2.60	5.95	2.10
$C_4H_9{-}C{\equiv}C{-}CH{=}CH_2$ (IV)	2.57	7.20	0.50
	2.56	7.33	1.06
$C_8H_{13}{-}C{\equiv}C{-}CH{=}CH_2$ (V)	2.55	11.60	0.43
	2.54	12.10	0.84
$CH{\equiv}C{-}C(CH_3){=}CH_2$ (VI)	2.51	5.25	1.31
	2.51	5.17	1.37
$CH{\equiv}C{-}C(C(CH_3)_3){=}CH_2$ (VII)	2.58	7.20	0.92
	2.59	7.25	1.62
$CH_3{-}C{\equiv}C{-}C(CH_3){=}CH_2$ (VIII)	2.80	6.24	1.10
	2.80	6.60	2.26
$CH_3{-}C{\equiv}C{-}C(C(CH_3)_3){=}CH_2$ (IX)	2.83	4.20	0.62
	2.84	4.13	1.31
$C_2H_5{-}C{\equiv}C{-}C(C(CH_3)_3){=}CH_2$ (X)	2.82	3.43	1.13
	2.82	3.74	2.26
$CH{\equiv}C{-}CH{=}CH{-}CH_3$ (XI)	2.61	7.30	1.24
	2.62	7.65	3.35
$CH{\equiv}C{-}C(CH_3){=}CH{-}CH_3$ (XII)	2.56	6.75	0.09
	2.55	7.30	1.72

The following conclusions may be derived from the data of this table.

1. Vinylacetylene is reduced somewhat more easily than divinyl and less easily than diacetylene [4]. Its half-wave potential is nearly the same as those of styrene and phenylacetylene [3, 4].

2. The nearest homologs of vinylacetylene are less easily reduced than unsubstituted vinylacetylene.

3. The position of a single methyl group has a slight effect on the reduction potential. The isomer with the methyl group in position 3 is most easily reduced.

4. Lengthening of the carbon chain in position 1 causes a slight decrease in the half-wave potentials (II-V). In the same way the half-wave potentials depend only slightly on whether there is a saturated or an unsaturated radical adjacent to the triple bond; divinylacetylene has about the same reduction potential as vinylethylacetylene [4].

5. When the length and degree of branching of the radical in position 3 are increased, the half-wave potential is somewhat increased (VI-VII).

6. The effect of two methyl groups on the half-wave potentials strongly depends on their position. The appearance of a second group adjacent to the double bond very slightly changes the half-wave potential (XII). If one of the methyl groups replaces hydrogen next to the acetylenic bond and the other replaces hydrogen next to the ethylenic bond, the reduction potential sharply increases (VIII).

* Allylmethylacetylene also was investigated. However, experiments showed that it is not reduced at the mercury electrode; the hydrocarbon does not have a conjugated system of multiple bonds.

These characteristics of the polarograms of vinylacetylenic hydrocarbons of different structures can be explained most easily by the effect of radicals on the possibility of hydrocarbon adsorption on the mercury surface. As in catalytic hydrogenation [1, 2], adsorption probably takes place most readily at the acetylenic bond, since replacement of hydrogen at the triple bond has a greater effect on the half-wave potentials than replacement at the double bond. Introduction of a methyl group into hydrocarbon (XI) in position 3 even lowers the half-wave potential somewhat. Apparently adsorption occurs at the ethylenic bond also, since substitution at the end of the ethylenic grouping has a greater effect on the half-wave potential than substitution on the middle carbon atom. This hypothesis is supported by the sharp increase in the half-wave potential on simultaneous replacement of hydrogens adjacent to the ethylenic and acetylenic bonds.

The absence of discontinuities in the polarographic curve indicates that hydrogenation by atomic hydrogen, in contrast to catalytic hydrogenation, is not selective.

At least four electrons take part in the hydrogenation of vinylacetylenes.*

EXPERIMENTAL

The polarographic investigation was conducted with a Type PV-5 visual polarograph. The Type M-21 mirror galvanometer had a sensitivity of 1×10^{-9} amp/mm/m.

A 0.1 M solution of tetrabutylammonium iodide in a 75% solution of dioxane in water was used as electrolyte. The tetrabutylammonium iodide was synthesized by the G. I. Mikhailov method [6] and recrystallized three times from anhydrous dioxane purified by boiling over metallic sodium [7]. The pure dioxane was kept in a refrigerator, and in the course of 10 days no appreciable quantities of peroxide were found on the polarogram.

The electrolysis cell contained 1 ml of solution, and was situated in a thermostat at 25 ± 0.1°. The cathode was a dropping mercury electrode, and the anode was a mercury layer whose potential was measured with a Type PPTV-1 potentiometer, and was equal to 0.406 ± 0.008 v with respect to the saturated calomel electrode (s.c.e.) for a 0.1 M solution of tetrabutylammonium iodide in 75% dioxane.

The capillary was purified by the Lambert method [8] and was kept in 1 N nitric acid when not in use. The open-circuit capillary characteristic $L = m^{2/3}t^{1/6} = 1.070$ $mg^{2/3} \cdot sec^{-1/2}$ and the mercury-dropping period t= 8 sec. The mercury pressure was 43 cm.

Two initial solutions (1 drop of the substance in 1 ml of 75% dioxane) were prepared for each substance; each solution was polarographed twice. Thus, four polarograms were taken for each substance. The concentrations of the substances being investigated varied from 0.0005 to 0.007 M. The galvanometer sensitivity was equal to 1/50.

The polarography was carried out in the presence of atmospheric oxygen, whose reduction wave lies in a more positive potential region than the waves of the substances investigated. The possibility of polarographic investigations in the presence of atmospheric oxygen has been pointed out in several works [9, 10].

The diffusion current for atmospheric oxygen in 75% dioxane at 25° has some definite value (Fig. 1).

In a study of vinylacetylenic hydrocarbons which are reduced in the region from −2.10 to −2.95 v (s.c.e.), a marked decrease in the diffusion current was observed as the potential of the dropping mercury electrode increased (Fig. 2). The same phenomenon was observed on the oxygen polarogram (Fig. 1). This decrease in the diffusion current is primarily due to a decrease in the mercury dropping period at high negative potentials, as follows from the Il'kovich equation [11].

We investigated the relation between the capillary characteristic and the applied voltage (Table 2). As is evident from the dependence of the capillary constant on the voltage, the capillary characteristic begins to decrease markedly at −2.0 v as a result of the decrease in the mercury dropping period; the mass of mercury flowing out in 1 sec remains constant [11]. Knowing the capillary characteristic at any potential relative to the mercury anode, one may calculate the values of diffusion currents, which correspond to the same capillary characteristic $m^{2/3}t^{1/6} = 1$.

*An approximate calculation of the number of electrons participating in the process was made by means of the Il'kovich equation [5]. The diffusion coefficients were arbitrarily taken to be equal to 1×10^{-5} cm^2/sec.

Treatment of the experimental data obtained, consisted in the following. The plotted diffusion currents of the hydrocarbons were dropped to the curve of the oxygen wave at the measuring points i_D and, moreover, were corrected by the amount of the decrease in diffusion current, due to the decrease in the dropping mercury period [12]. For this the corrected value of the current was determined at a series of points on the polarogram, and a new, corrected polarogram was constructed (Fig.2).

TABLE 2

Relation Between the Capillary Constant and the Potential*

E_{Hg} (v)	m (mg/sec)	t (sec)	$m^{2/3} t^{1/6}$ ($mg^{2/3} \cdot sec^{1/2}$)
0	0.650	8.0	1.070
0.4	0.645	8.36	1.064
0.8	0.644	7.48	1.035
1.2	0.648	6.42	1.022
1.6	0.651	5.19	0.990
1.8	0.660	4.70	0.976
2.0	0.663	3.85	0.952
2.2	0.663	2.63	0.918
2.4	0.661	1.99	0.850
2.5	0.663	1.47	0.815
2.58	0.664	0.96	0.757
2.60	0.664	0.83	0.740
2.66	0.663	0.52	0.684

* A 0.1 M solution of $(C_4H_9)_4$ NI in 75% dioxane. Hg pressure 43 cm. Temperature 16°. E_{Hg} corrected for the potential drop across the resistance of the electrolytic circuit.

The value of the corrected current was determined by the formula

$$i_{corr} = \frac{i_t - i_{O_2}}{L}$$

where i_{corr} is the corrected current, i_t is the total current for oxygen and the substance being investigated at the potential to which the capillary characteristic L corresponds; i_{O_2} is the current for oxygen at the same potential.

The corrected diffusion current for hydrocarbons (VIII-X) was about 40% greater than the experimental.

The diffusion current constants are given in Table 1.

$$I_D = \frac{i_{Dcorr}}{C}$$

The half-wave potentials were determined with an accuracy of ± 0.02 v by means of the graphical relation between $\log[i_{corr}/(i_{dcorr}-i_{corr})]$ and $E_{s.c.e.}$ and was corrected for the potential drop across the ohmic resistance of the electrolytic circuit $\Delta E = Ri_{dt}$, where R is the circuit resistance, equal to 6000 ohms,* and i_{dt} is the total diffusion current, equal to the sum of the diffusion currents for oxygen and the substance being investigated.

For hydrocarbons (I-VII) and (XI-XII) in the concentration interval investigated, the diffusion current is directly proportional to the concentration. Hydrocarbons (VIII-X) do not give a sufficiently clear diffusion-current plateau at concentrations greater than 0.003 M.

The effect of temperature on the diffusion current also was investigated. The measurements were made at 16 and 25°. The temperature coefficients for all hydrocarbons were about the same (approximately 1.4% per degree).

The angular coefficients in the wave equation, defined as the cotangents of the angles of inclination of the straight lines expressing the wave equation plotted in the coordinates $\log[i_{corr}/(i_{dcorr}-i_{corr})]$ and $E_{s.c.e.}$, were considered. The apparent number of electrons taking part in reduction, which was determined from the angular coefficients, is equal to 0.5. Since at least two electrons participate in the reduction process, reduction in the present case should be considered irreversible [9].

In order to check the method used, we took a polarogram of styrene at a concentration of 0.003 M with a background of 0.175 M tetrabutylammonium iodide in 75% dioxane in the presence of atmospheric oxygen. The half-wave potential $E_{1/2}$ (corrected for the potential drop across the resistance of the electrolytic circuit) was found to be −2.33 v (s.c.e.), which is close to the value obtained for styrene under the same conditions but in a nitrogen atmosphere (−2.34 v) [14].

*The resistance of the electrolytic circuit was determined by means of a Type R-38 slide-wire bridge. An EO-7 oscillograph was used as zero indicator. The alternating-current source was a ZG-10 sound generator. The measurements were made at 1000 cycles and 2 v [13].

Methods of preparation of all hydrocarbons used in the present work are described in the preceding articles [15].*

SUMMARY

1. The polarographic reduction of 12 vinylacetylenic hydrocarbons of different structures was investigated.

2. It was shown that substitution of hydrogen atoms by alkyl groups increases the half-wave potentials, especially if this substitution takes place next to both multiple bonds.

3. Not more than one wave could be found on any of the polarograms, although at least four electrons apparently take part in the process.

LITERATURE CITED

[1] A. A. Petrov, Kh. V. Bal'yan, and Yu. I. Porfir'eva, Zhur. Obshchei Khim. 26, 1926 (1956);** 27, 365 (1957).**

[2] Kh. V. Bal'yan and N. A. Borovikova, Zhur. Obshchei Khim. 29, 2882 (1959).**

[3] A. P. Terent'ev and L. A. Yanovskaya, "The polarographic method in organic chemistry." Collection: Reactions and Methods of Investigation of Organic Compounds [in Russian], No. 5 (Goskhimizdat, 1957).

[4] M. Stackelberg and W. Stracke, Z. Elektroch. 53, 118 (1949).

[5] D. Il'kovich, Coll. Czechoslov. Commun. 6, 498 (1934).

[6] G. I. Mikhailov, Zhur. Priklad. Khim. 27, 217 (1954).**

[7] R. A. Burdett and B. E. Gordon, Anal. Chem. 19, 843 (1947).

[8] F. L. Lambert, Anal. Chem. 46, 10 (1957).

[9] A. G. Stromberg and A. G. Pozdeeva, Zhur. Obshchei Khim. 20, 54 (1950).**

[10] A. G. Pozdeeva and A. G. Volkov, Zhur. Priklad. Khim. 25, 1052 (1952).**

[11] I. M. Kolthoff and J. J. Lingane, Polarography [Russian translation]. (IL, 1948).

[12] L. H. Chopard-dit-Jean and E. Heilbronner, Helv. Chim. Acta 36, 144 (1953).

[13] M. R. Peske, S. L. Knesbach, and R. K. Ladisch, Anal. Chem. 25, 979 (1953).

[14] H. A. Laitinen and A. Wawzonek, J. Am. Chem. Soc. 64, 1765 (1942).

[15] A. A. Petrov, K. S. Mingaleva, et al., Doklady Akad. Nauk SSSR 123, 298 (1958); Zhur. Obshchei Khim. 29, 3732 (1959).**

* The authors express their thanks to B. S. Kupin and Yu. I. Porfir'eva for providing some of the hydrocarbons investigated.

** Original Russian pagination. See C. B. translation.

INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

CXI. ON THE ORDER OF ADDITION OF TERTIARY ALKYL HALIDES TO VINYLACETYLENE*

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 3992-3999, December, 1959

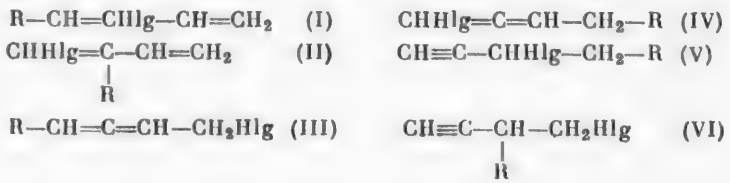
Original article submitted December 23, 1958

Earlier it was shown that in the presence of zinc halides, tertiary-butyl bromide and chloride add to vinylacetylene at the acetylenic bond, to form 2-halo-1-tert-butylbutadienes-1,3 [1]. The conclusion on the indicated structure of the addition products was reached on the basis of a study of their ozonolysis, and also their Raman spectra.

The ozonization method made it possible to judge the structure of the main substance alone. Slight admixtures of isomers could be ignored. The Raman spectra permitted one, with complete certainty to exclude the possibility of the presence of substances with formulas (V) and (VI) in the reaction products, since the line of the acetylenic bond has high intensity in Raman spectra. The detection of slight admixtures of allenic isomers by this method is unreliable.

In this article we give additional data on the structure of the addition products of tertiary-alkyl halides with vinylacetylene. Addition reactions of four tertiary-alkyl chlorides, four bromides, and two iodides with vinylacetylene in the presence of zinc halides were investigated. The reaction time in all cases was measured for several days. The iodides reacted most easily and the chlorides, with the greatest difficulty. Yields of the simple adducts varied from 30 to 65%, depending on the nature of the alkyl halide and the reaction time. They were highest in the case of iodides (40-65%). Besides the simple adducts, higher-boiling substances were always obtained in amounts from 10 to 40% of the weight of the reaction products. Their yield was least in the case of iodides. To determine the structure of the addition products of alkyl halides with vinylacetylene their infrared spectra and reduction reactions on $Pd/CaCO_3$ were used.

In the infrared spectra of the bromides and iodides the lines of the acetylenic (3300 and 2100 cm^{-1}) and allenic (1960 cm^{-1}) groupings were completely absent. These substances absorbed as typical 1,3-diene compounds. The dienic character of the addition products was indicated by other properties of theirs, in particular, their exceptional stability toward alcoholic alkali. Thus, the bromides and iodides could have only formulas (I) or (II).



*Enyne compounds. XXXIV.

TABLE 1

Substance	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated
$(CH_3)_3C-CH=CCl-CH=CH_2$	43—44° (10)	0.9077	1.4755	44.90	43.08
$(CH_3)_2C(C_2H_5)-CH=CCl-CH=CH_2$	61.5—62 (10)	0.9230	1.4834	49.13	47.70
$(C_2H_5)_2C(CH_3)-CH=CCl-CH=CH_2$	80—80.5 (10)	0.9261	1.4870	53.63	52.31
$(C_2H_5)_3C-CH=CCl-CH=CH_2$	91—92 (10)	0.9349	1.4938	58.12	56.93
$(CH_3)_3C-CH=CBr-CH=CH_2$	57—58 (10)	1.1686	1.5012	47.69	45.98
$(CH_3)_2C(C_2H_5)-CH=CBr-CH=CH_2$	72—72.5 (10)	1.1667	1.5070	51.84	50.59
$(C_2H_5)_2C(CH_3)-CH=CBr-CH=CH_2$	88—88.5 (10)	1.1485	1.5090	56.36	55.21
$(C_2H_5)_3C-CH=CBr-CH=CH_2$	103—104 (10)	1.1405	1.5122	60.86	59.83
$(CH_3)_3C-CH=CI-CH=CH_2$	73.5—74.5 (10)	1.4185	1.5419	52.37	51.01
$(CH_3)_2C(C_2H_5)-CH=CI-CH=CH_2$	63.5—64 (4)	1.3963	1.5446	56.60	55.63

When the addition product of tertiary-butyl bromide was reduced on $Pd/CaCO_3$, there was obtained only 2,2-dimethylhexane without admixture of the other possible isomer (2,2,3-trimethylpentane). We verified this by comparing the infrared spectra of the two expected hydrocarbons with the spectrum of the hydrogenation products. Thus it was shown, that the addition of alkyl bromides, at least, to vinylacetylene goes only in one previously assumed direction — with the formation of 2-halo-1-tert-alkylbutadienes-1, 3.

We were unable to reduce the corresponding iodide; however, we think that the conclusion reached for bromides is also applicable to iodides.

In the infrared spectra of the addition products of tertiary-alkyl chlorides with vinylacetylene, lines of the terminal acetylenic grouping are also completely absent; along with intense lines of the 1,3-diene system, however, there is a low- or medium-intensity line of the allene system (Fig. 1). Thus, in this case addition goes in two directions: mainly to the acetylenic bond and, to a slight degree, to the 1,4-position.

The amount of allenes decreased as the reaction time increased, but not to zero. In the same way allenes were not completely eliminated on treatment of the adducts with sodium alkoxides or the sodium salt of glycol. Formula (III) may be assigned with certainty to the unstable allenes and formula (IV), apparently, to the stable ones. The amount of the latter is small (of the order of 5%).

On reduction of the tertiary-butyl chloride addition product on $Pd/CaCO_3$, only 2,2-dimethylhexane was obtained. Therefore, the structure of the carbon skeleton in the dienic and allenic chlorides is the same: Formulas (II) and (VI) were certainly excluded for both isomers.

The formation of two alkyl chloride adducts suggests that possibly the reaction goes in two directions in other cases, but in the case of bromides and iodides the 1,4-adduct is isomerized to the more stable 1,3-dienic adduct, whereas, in the case of chlorides part of the allenic adduct remains.

As noted above, in all cases we obtained, along with the simple adducts, a certain amount of tarry, higher-boiling substances. The latter could be either higher telomers, formed at the expense of allenic addition products of Type (III) (1,3-dienic halides cannot telomerize, since they contain a halogen atom of low mobility), or polymers of the main adducts. The tendency of these substances toward polymerization was noted by us in the preceding article.

Investigation of the infrared spectra of the higher fractions of methyldiethylchloro- and bromomethane adducts showed that these fractions contain mainly ethylenic bonds and, to a very slight degree, allenic ones.

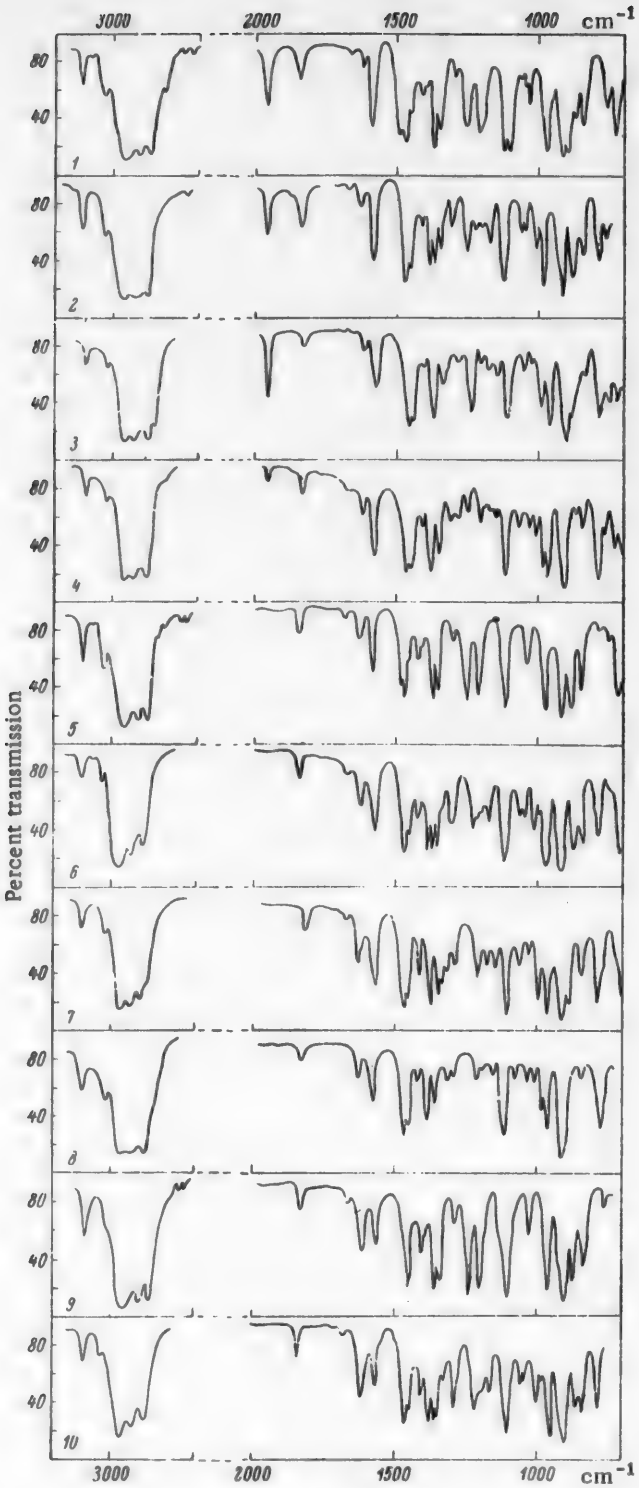


Fig. 1. Infrared transmission spectra of adducts of tertiary-alkyl halides to vinylacetylene. 1) 3-Chloro-5,5-dimethylhexadiene-1,3; 2) 3-chloro-5,5-dimethylheptadiene-1,3; 3) 3-chloro-5-methyl-5-ethylheptadiene-1,3; 4) 3-chloro-5,5-diethylheptadiene-1,3; 5) 3-bromo-5,5-dimethylhexadiene-1,3; 6) 3-bromo-5,5-dimethylheptadiene-1,3; 7) 3-bromo-5-methyl-5-ethylheptadiene-1,3; 8) 3-bromo-5,5-diethylheptadiene-1,3; 9) 3-iodo-5,5-dimethylhexadiene-1,3; 10) 3-iodo-5,5-dimethylheptadiene-1,3.

Thus, they apparently are formed by both of the routes indicated above, but mainly by polymerization, the latter proceeding primarily through 1,4 addition (the intensity of the 956 cm^{-1} line is much greater than that of the 989 cm^{-1} line).

Besides zinc halides, we attempted to use other catalysts in the reaction, (ones which had proved effective in telomerization with the participation of dienic hydrocarbons, e.g., stannic chloride [2]). However, the results were poorer than with zinc halides; the reaction was much more rapid, but the yield of simple adducts was small. The tertiary-butyl chloride adduct contained twice as much of the allenic chloride as that obtained with zinc chloride. Attempts at addition of primary and secondary halides to vinylacetylene in the presence of the same catalysts were unsuccessful. Attempts at splitting-out of hydrogen halides from chlorides, bromides, and iodides by treatment with KOH in methanol, glycol, or diethylene glycol at the boiling points of these solvents also were unsuccessful; either the splitting-out of hydrogen halides went too slowly or polymeric products were obtained.

The constants of the adducts obtained are compared in Table 1.

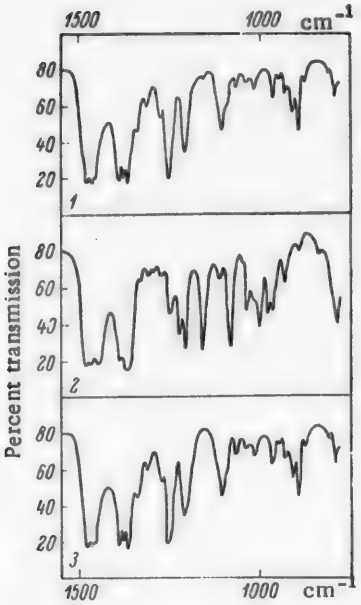


Fig. 2. Infrared transmission spectra. 1) Hydrogenation product of the adduct of tertiary-butyl chloride with vinylacetylene; 2) 2,2-dimethylhexane; 3) 2,2,3-trimethylpentane.

From the data of Table 1 it is evident that the refractive indices in all cases increase with the size of the radical, whereas the specific gravity increases for a number of chlorides and decreases for the rest of the cases. The molecular exaltation is greatest for chlorides, and decreases on increase of the radical size.

In Fig. 1 are shown the infrared spectra of the substances obtained. In the literature there are few data on the infrared spectra of 1,3-dienic halo derivatives. The spectra of chloroprene [3], bromoprene [4], 1-bromobutadiene, and certain dibromides [4] and perchlorides [3] have been studied. The present investigation confirmed the regularities found earlier in the spectra of other dienic halo-derivatives, as well as hydrocarbons with substitution of a similar character.

1) The conjugated system of double bonds is characterized by two lines: 1580 and 1620 cm^{-1} in the case of chlorides, 1575 and 1625 cm^{-1} in that of bromides, and 1570 and 1620 cm^{-1} in that of iodides. Thus, the wave number of the unsymmetrical vibrations decreases somewhat on transition from chlorides to iodides. In contrast to the case of chloroprene and bromoprene, this line is much more intense than that of symmetrical vibrations in the case of the chlorides and bromides described in the present work.

2) The vinyl group is characterized by two lines of nonplanar CH deformation vibrations (910-916 and 966-972 cm^{-1}). Both lines have lower wave numbers than the corresponding lines in olefins, as was noted earlier for other compounds with conjugated multiple bonds. The line of lower wave number has a very high intensity, probably owing to the superposition of CC vibration lines of the quaternary carbon atom. The characteristic overtone of low intensity at about 1835 cm^{-1} corresponds to this line. The low-intensity lines at about 1410-1415 cm^{-1} correspond to symmetrical deformation vibrations in the $=CH_2$ group. The lines in the 3000-3100 cm^{-1} region correspond to CH valence vibrations.

3) The intense 1205 and 1245 cm^{-1} lines correspond to CC vibrations in the tertiary-butyl radical. The first of them coincides with a line also observed in the spectra of haloprenes. Only compounds with this radical have planar CH vibrations with a high wave number, about 1475 cm^{-1}. When branching occurs at the third carbon atom, lines appear in the spectrum in the 990-1100, 1060, 1150, 1380, and 1450 cm^{-1} regions, and the lines characteristic of the quaternary carbon atom in the 1200-1250 cm^{-1} region remain.

EXPERIMENTAL

Experiments with zinc halides as catalysts were performed under identical conditions. A mixture of an alkyl halide and vinylacetylene in nearly equimolar quantities was shaken for several days in the presence of a few percent of one of the above-mentioned catalysts. Then a small amount of diethylamine or pyridine, enough to take up the catalyst, was added. After filtration the mixture was distilled in vacuo. The reaction conditions and yields of addition products are given in Table 2.

TABLE 2

Alkyl halide	Taken			Time (in days)	Obtained (in g)		Yield of adduct (in %)
	C_4H_4 (in moles)	RHlg (in moles)	$ZnHlg_2$ (in g)		adduct	residue	
$(CH_3)_3C-Cl$	0.4	0.6	1.4	9	24.5	9.5	42
$(CH_3)_2(C_2H_5)C-Cl$	0.6	0.7	3.5	5	31.7		33
$(C_2H_5)_2(CH_3)C-Cl$	0.3	0.3	1.5	7	15.5	4.0	30
$(C_2H_5)_3C-Cl$	0.14	0.14	1.5	7	11.0	7.0	42
$(CH_3)_3C-Br$	0.52	0.57	2.0	4	44.0	13.0	45
$(CH_3)_2(C_2H_5)C-Br$	0.2	0.2	1.5	5	13.5	2.5	38
$(C_2H_5)_2(CH_3)C-Br$	0.26	0.26	3.0	4	33.7	9.5	60
$(C_2H_5)_3C-Br$	0.1	0.1	1.5	4	11.7	6.4	51
$(CH_3)_3C-I$	0.14	0.14	0.8	5	21.0	2.5	65
	0.14	0.14	0.8	4	15.7	1.8	49
$(CH_3)_2(C_2H_5)C-I$	0.1	0.1	1.0	4	10.0	1.5	40

In an experiment using stannic chloride as catalyst, the following results were obtained. There were taken 0.75 mole of vinylacetylene and 0.75 mole of tertiary-butyl chloride in 40 ml of methylene chloride. A 1.6 g quantity of stannic chloride, dissolved in CH_2Cl_2, was added. The mixture was stirred for 25 hours at −5 to −10°. After addition of pyridine and filtration, the mixture was fractionated in vacuo. There was obtained 11.3 g of a substance with b. p. 35-43° (10 mm), the main fraction of which (8.5 g) had the following constants: b. p. 43.5-44° (10 mm), d_4^{20} 0.9146, n_D^{20} 1.4752.

Besides, 30.2 g of a higher-boiling, tarry residue was obtained.

On treatment of a sample of the main fraction with boiling methanolic KOH solution for 45 minutes, about 20% of the chlorine in the sample went into solution. In a similar experiment with the product obtained in the presence of zinc chloride, 12% of the chlorine went into solution.

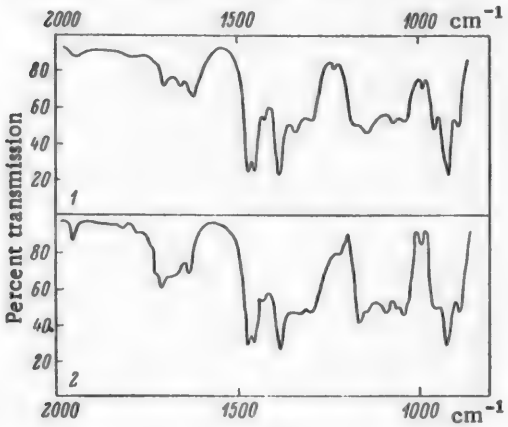


Fig. 3. Infrared transmission spectra of residues left after distillation of the addition products of dimethylethylchloro-(1) and -bromomethanes (2) with vinylacetylene.

Analytical data for the newly prepared substances are given in Table 3.

The infrared spectra were taken with an IKS-14 spectrograph using LiF and NaCl prisms, with a layer thickness of 0.033 mm. Data are shown in Figs 1 and 2.

On hydrogenation of 10.49 g of $(CH_3)_3C-CH=CCl-CH=CH_2$ in 40 ml of CH_3OH in the presence of 15 g of $Pd/CaCO_3$ (Pd content 0.006 g per g of catalyst), 4350 ml of H_2 (765.6 mm, 20°) was absorbed. The reaction products were steam distilled and then salted out with saturated $CaCl_2$ solution. There was obtained 4.2 g (50%) of 2,2-dimethylhexane. B. p. 106-107°, d_4^{20} 0.6958, n_D^{20} 1.3950, which corresponds to literature data [5]. The infrared spectrum of the substance is shown in Fig. 3.

$(CH_3)_3C-CH=CBr-CH=CH_2$ was similarly reduced.

The yield of 2,2-dimethylhexane was 52%. The constants and infrared spectrum did not differ from those given above.

Known 2,2-dimethylhexane was prepared by treating tertiary-butyl bromide with butylmagnesium bromide in ethereal solution in the presence of Cu_2Br_2. B. p. 106-107°, d_4^{20} 0.6964, n_D^{20} 1.3955 [5].

The isomeric hydrocarbon, 2,2,3-trimethylpentane, was prepared by hydrogenation on $Pd/CaCO_3$ of the dehydration product (obtained by distillation with oxalic acid solution) of methylethyl-tert-butylcarbinol (obtained from pinacoline and ethylmagnesium bromide). B. p. 109-110°, d_4^{20} 0.7165, n_D^{20} 1.4041, which corresponds to literature data.

TABLE 3

Substance	Found (%)			Calculated (%)		
	C	H	Hlg	C	H	Hlg
$(CH_3)_2C(C_2H_5)-CH=CCl-CH=CH_2$	68.35, 68.36	9.62, 9.65	22.17, 22.47	68.13	9.53	22.35
$(C_2H_5)_2C(CH_3)-CH=CCl-CH=CH_2$	69.65, 69.38	9.91, 10.01	20.64, 20.81	69.56	9.91	20.54
$(C_2H_5)_3C-CH=CCl-CH=CH_2$	70.95, 71.02	10.36, 10.19	18.76, 18.49	70.75	10.26	18.99
$(CH_3)_2C(C_2H_5)-CH=CBr-CH=CH_2$	53.44, 53.25	7.66, 7.52	39.20, 39.37	53.21	7.44	39.34
$(C_2H_5)_2C(CH_3)-CH=CBr-CH=CH_2$	55.41, 55.64	7.70, 7.76	37.06	55.81	7.89	36.80
$(C_2H_5)_3C-CH=CBr-CH=CH_2$	57.33, 57.76	8.33, 8.36	34.64	57.15	8.28	34.57
$(CH_3)_2C-CH=CI-CH_2=CH_2$	40.66, 40.63	5.58, 5.71	53.42, 53.56	40.70	5.55	53.76
$(CH_3)_2C(C_2H_5)-CH=CI-CH=CH_2$	42.60	6.16	51.17, 51.26	43.21	6.05	50.74

The infrared spectrum of this hydrocarbon is distinguished from that of 2,2-dimethylhexane by the presence of intense lines at 1080 and 1155 cm^{-1}.

SUMMARY

1. Reactions of addition of 10 tertiary alkyl halides to vinylacetylene in the presence of zinc halides were studied.

2. It was shown that in the case of bromides and iodides, addition takes place only at the acetylenic bond. In the case of chlorides 1,4- addition also is observed.

3. It was found that when the adducts are reduced on $Pd/CaCO_3$, the corresponding saturated hydrocarbons with a quaternary carbon atom are obtained.

4. In the infrared spectra of the adducts there are regularities due to the presence of a 1,3-diene system and tertiary radicals.

LITERATURE CITED

[1] A. A. Petrov and K.V. Leet-s, Doklady Akad. Nauk SSSR 95, 285 (1954).

[2] A. A. Petrov, N. A. Razumova, and M. L. Genusov, Zhur. Obshchei Khim. 28, 1128, 2132, 3220 (1958).*

[3] G. J. Szasz, and N. Sheppard, Trans. Farad. Soc. 49, 358 (1953).

[4] A.A. Petrov G. I. Semenov, and N. P. Sopov, Zhur. Obshchei Khim. 27, 928 (1957).*

[5] R. D. Obolentsev, Physical Constants of Hydrocarbons [in Russian], (Gostoptekhizdat, 1953).

*Original Russian pagination. See C. B. translation.

INVESTIGATIONS ON CONJUGATED SYSTEMS

CXII. THE DIRECTION OF HYDRATION OF ALLYLMETHYLACETYLENE (1-HEXEN-4-YNE)*

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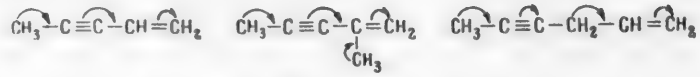
Translated from Zhurnal Obshchei Khimii, Vol 29, No. 12, pp. 3999-4002,

December, 1959

Original article submitted December 23, 1958

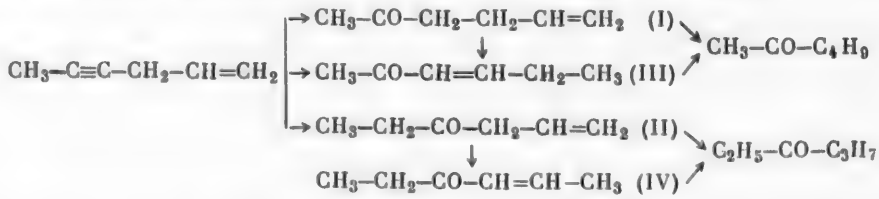
Vinyl- and isopropenylacetylenes add water under the conditions of the Kucherov reaction in different ways: vinylalkylacetylenes form alkylpropenyl ketones, whereas isopropenylalkylacetylenes give alkylisopropenyl ketones [1-3]. The shift of the electron cloud in the molecules of these hydrocarbons under the influence of radicals should be in the same direction [4, 5].



For elucidation of the causes of the above behavior, it was necessary to study the hydration of hydrocarbons of similar structure containing an unconjugated system of multiple bonds. We therefore continued our work on the relation between structure and reactivity of vinylacetylenic hydrocarbons by studying the hydration of allylmethylacetylene (1-hexen-4-yne). The latter, like vinylmethylacetylene, does not contain a conjugated system of multiple bonds.

This reaction has not been studied before. Homologs of allylmethylacetylene have been investigated with reference to the addition of alcohols in presence of BF_3 which apparently goes with formation of ketals $RC(OR)_2CH_2CH_2CHCH_2$, although the structure of the latter has not yet been conclusively established [6].

Hydration of allylmethylacetylene can be expected to give two isomeric ketones (I) and (II); ketone (II) (ethylallyl ketone) could readily isomerize to ketone (IV) (ethylpropenyl ketone) containing a conjugated system of double bonds [7]. A similar isomerization is possible for ketone (I) but is less probable.



Ketone (I) (1-hexen-5-one) was actually found to be the predominating product. Its double bond and carbonyl group are not conjugated.

The constants of the product of hydration of allylmethylacetylene only differed slightly from those cited in the literature for 1-hexen-5-one and differed considerably from the constants of ketones (II) to (IV). The melting point of the 2,4-dinitrophenylhydrazone of the isolated ketone was also identical with that of the 2,4-dinitrophenylhydrazone of 1-hexen-5-one and differed considerably from the melting points of the other possible isomeric ketones.

* Enyne compounds. XXXV.

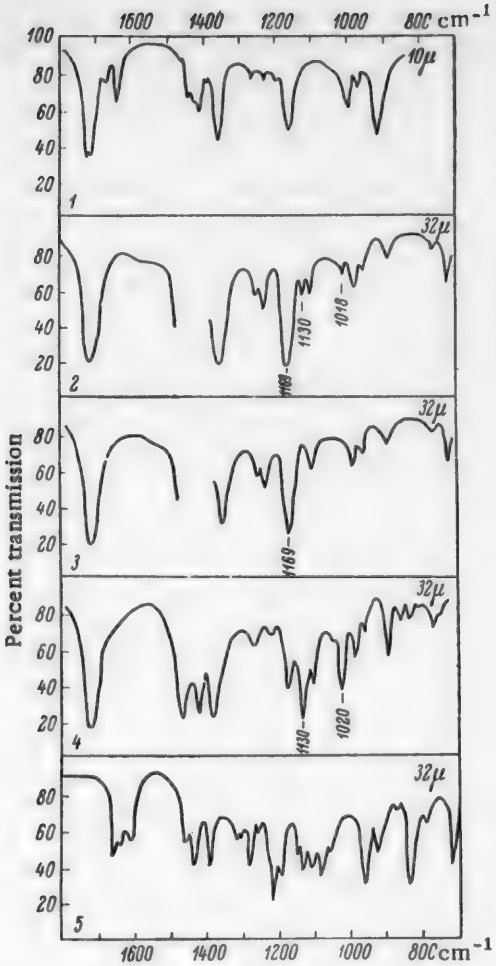


Fig. 1. Infrared transmission spectra. 1) Mixture of ketones obtained on hydration of allylmethylacetylene; 2) mixture of ketones obtained on hydrogenation of products of hydration; 3) methylbutyl ketone; 4) ethylpropyl ketone; 5) products of addition of methyl alcohol to allylmethylacetylene.

On the evidence of the infrared and ultraviolet spectra, however, 1-hexene-5-one is accompanied by a trace of a ketone with conjugated double bonds (Figs. 1 and 2).

The infrared spectrum contains, in addition to the strong bands of the unconjugated carbonyl group (1710-1720 cm^{-1}) and of the vinyl group (915 and 995 cm^{-1}), weak frequencies that could be associated with traces of ketones (III) or (IV). The latter contain conjugated double bonds (1676 cm^{-1} is the frequency of the conjugated carbonyl, 972 cm^{-1} is the frequency of the $-CH = CH-$ grouping).

The ultraviolet spectrum contains, in addition to the maximum at 270 mμ characteristic of the unconjugated carbonyl bond, a maximum at 220 mμ characteristic of conjugated ketones. •

Quantitative data for the composition of the products of hydration were obtained by investigation of their catalytic hydrogenation. The constants of the hydrogenation product hardly differed from those of pure methylbutyl ketone. The 2,4-dinitrophenylhydrazone had the same melting point as methylbutyl ketone 2,4-dinitrophenylhydrazone.•• However, the infrared spectrum of the hydrogenation products (Figs. 1 and 2) contained two weak frequencies (1130 and 1017 cm^{-1}) absent from the spectrum of pure methylbutyl ketone and prominent in the spectrum of ethylpropyl ketone (Fig. 1, Curves 3 and 4). The infrared spectrum of the products of hydrogenation was identical with the spectrum of a mixture of 85% methylbutyl ketone and 15% ethylpropyl ketone.•••

Comparison of these data with those for the infrared and ultraviolet spectra of the original mixture of unsaturated ketones led to the conclusion that hydration of allylmethylacetylene gives about 85% of ketone (I) and 15% of ketone (IV).

The sequence of addition of methyl alcohol to allylmethylacetylene in presence of KOH was the same as that of water. An enolic ether was formed whose infrared spectrum (Fig. 1, Curve 5) conclusively pointed to the presence of a vinyl group (frequencies 927 and 961 cm^{-1}) and a $-CH = C<$ group (frequency 830 cm^{-1}). On hydrolytic cleavage it gave predominantly 1-hexen-5-one which was reduced over $Pd/CaCO_3$ to methylbutyl ketone (identified as the 2,4-dinitrophenylhydrazone).

It has thus been established that the preferred direction of the reaction during hydration and addition of alcohols to allylmethylacetylene is the formation of 1-hexen-5-one or its enolic ethers. This is the same pattern of reaction as in the addition of water and alcohols to vinylalkylacetylenes. Consequently, the specific orientation in reactions of vinylalkylacetylene with water and alcohols is not determined exclusively by π,π-conjugation,

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• Here we are comparing the strong band of the conjugated carbonyl and the weak unconjugated carbonyl band. The strong unconjugated carbonyl band is in the vacuum ultraviolet [8].

•• The 2,4-dinitrophenylhydrazone of ethylpropyl ketone melts more than 20° higher than the 2,4-dinitrophenylhydrazone of methylbutyl ketone.

••• This determination was accurate to within 2-3%.

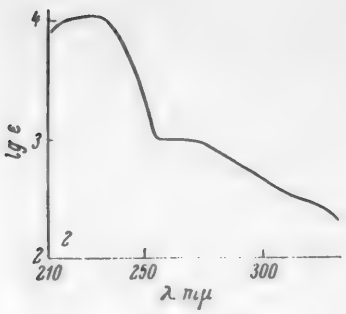

Fig. 2. Ultraviolet spectrum of the mixture of ketones obtained on hydration of allylmethylacetylene.

as we had previously assumed [2, 3], but is bound up with other factors that call for further investigations.

EXPERIMENTAL

Allylmethylacetylene was prepared by Grignard synthesis from methylacetylene and allyl bromide [9].

Hydration. 17 g of the hydrocarbon was vigorously stirred for 10 hr with a solution of 6 g mercuric oxide in 350 ml of 12% sulfuric acid. The upper layer, mainly ketone and unreacted hydrocarbon, was separated. Ketone was salted out from the lower layer with ammonium sulfate and also separated. A total of 14 g of product was obtained. Distillation at normal pressure gave 1.8 g of initial fraction (mainly original hydrocarbon), 9.5 g ketones (51% yield on the reacted hydrocarbon) and 2.5 g residue.

The following data were obtained for the ketones:

B. p. 128-130°, 66-68° (100 mm), d_4^{20} 0.8444, n_D^{20} 1.4220.

Found %: C 73.47, 73.43; H 10.27, 10.22. $C_8H_{10}O$. Calculated %: C 73.47, H 10.20.

Infrared spectrum: 915 very strong, 972 weak, 995 strong, 1162 very strong, 1200 weak, 1266 weak, 1361 very strong, 1412 medium, 1424 medium, 1441 medium, 1464 weak, 1640 medium, 1676 weak, 1230 weak, 1711 very strong, 1720 very strong (cm^{-1}).

Ultraviolet spectrum: λ_{max} 220 and 270 mμ.

2,4-Dinitrophenylhydrazone: m. p. 105° (from alcohol) [10].

Four g of ketone in 15 ml of methanol was hydrogenated in presence of 6 g of $Pd/CaCO_3$. 967 ml H_2 (761.5 mm, 20°) was absorbed in the course of 30 min, corresponding to 96.7% of the theoretical. The reaction mixture was decanted from catalyst, and diluted with ether, and the solution was washed with saturated $CaCl_2$ solution. Distillation of the ether left a residue which gave the following fractions: 1st up to 125°, 0.4 g; 2nd 125-126°, 2.3 g (d_4^{20} 0.8047, n_D^{20} 1.4022), residue 0.4 g.

Infrared spectrum (2nd fraction): 723 medium, 768 weak, 887 weak, 957 weak, 985 medium, 1018 weak, 1105 weak, 1130 weak, 1169 strong, 1232 medium, 1256 medium, 1358 very strong, 1415 strong, 1463 strong, 1713-1721 very strong (cm^{-1}).

2,4-Dinitrophenylhydrazone: m. p. 106-107° (from alcohol), identical with that of methylbutyl ketone [11].

Addition of methyl alcohol. Three glass tubes were each charged with 4 g allylmethylacetylene, 4.8 g methyl alcohol and 2.8 g KOH powder. The tubes were sealed and heated for 7 hr at 150°. The contents were then distilled with steam. The upper layer of distillate was collected, washed with saturated $CaCl_2$ solution and dried over fused potassium carbonate.

Distillation of the substance at 100 mm gave about 4 g of unreacted hydrocarbon, 2 g of methylhexadiene ether, 1.5 g of fraction with b. p. 105-110°, and 2 g of residue.

Methylhexadiene ether (predominantly 2-methoxy-2,5-hexadiene): b. p. 77-78° (100 mm), d_4^{20} 0.8431, n_D^{20} 1.4714.

Found %: C 74.84, 74.72; H 10.39, 10.43. $C_7H_{12}O$. Calculated %: C 75.00; H 10.71.

Infrared spectrum: 719 medium, 789 weak, 830 strong, 927 medium, 961 strong, 1051 weak, 1085 medium, 1100 medium, 1133 medium, 1149 weak, 1193 medium, 1214 very strong, 1226 weak, 1254 very weak, 1282 medium, 1311 very weak, 1320 very weak, 1390 medium, 1432 medium, 1460 medium, 1610 medium, 1644 strong, 1660 strong cm^{-1}.

0.5 g of the ether was shaken for 1 hr with 10 ml 7% sulfuric acid. The mixture was thereupon saturated with ammonium sulfate; the ketone was collected (0.3 g) and subjected (without distillation) to hydrogenation over $Pd/CaCO_3$ in 5 ml methyl alcohol. 59 ml H_2 (777 mm, 19°) was absorbed, equivalent to 92.5% of the calculated quantity. Treatment of the hydrogenation product with 2,4-dinitrophenylhydrazine gave methylbutyl ketone 2,4-dinitrophenylhydrazone with m. p. 107-108°. No depression in admixture with an authentic specimen.

SUMMARY

1. The main product of hydration of allylmethylacetylene in the conditions of the Kucherov reaction is 1-hexen-5-one.

2. Addition of an alcohol to allylmethylacetylene in presence of KOH follows the same direction with formation predominantly of 2-methoxy-2,5-hexadiene.

LITERATURE CITED

[1] A. A. Petrov and B. S. Kupin, Zhur. Obshchei Khim. 28, 1998 (1958).•

[2] B. S. Kupin and A. A. Petrov, Zhur. Obshchei Khim. 29, 1151 (1959).•

[3] B. S. Kupin and A. A. Petrov, Zhur. Obshchei Khim. 29, 3738 (1959).•

[4] A. A. Petrov, K. S. Mingaleva, and B. S. Kupin, Doklady Akad. Nauk SSSR 123, 298 (1958).•

[5] A. A. Petrov, B. S. Kupin, T. V. Yakovleva, and K. S. Mingaleva, Zhur. Obshchei Khim. 29, 3732 (1959).•

[6] D. B. Killian, G. F. Hennion, and J. A. Nieuwland, J. Am. Chem. Soc. 58, 892 (1931).

[7] I. N. Nazarov and I. I. Zaretskii, Zhur. Obshchei Khim. 27, 624 (1957).•

[8] A. E. Gillam and E. S. Stern, Electronic Spectra [Russian translation] (IL, 1957) pp. 78, 134.

[9] A. A. Petrov, Zhur. Obshchei Khim. 26, 3319 (1956).•

[10] H. B. Wood and E. C. Horning, J. Am. Chem. Soc. 75, 5511 (1953).

[11] C. C. Hobbs and B. Hauston, J. Am. Chem. Soc. 76, 1254 (1954).

•Original Russian pagination. See C. B. translation.

THE INTERACTION OF AMINES WITH DERIVATIVES OF α-BROMOACRYLIC ACID

II. THE PROBLEM OF THE REACTION MECHANISM*

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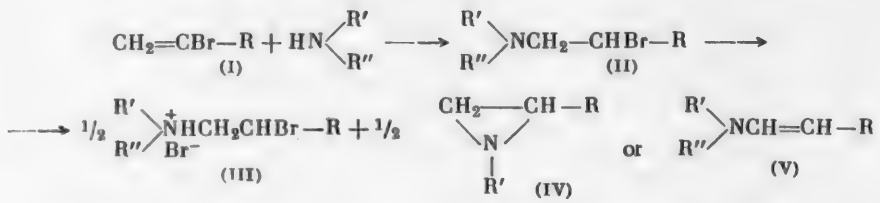
Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 12, pp. 4003-4010,

December, 1959

Original article submitted December 17, 1958

In the preceding communication [1] we showed that reaction of equimolar quantities of methylamine, benzylamine or piperidine with methyl α-bromoacrylate leads to formation of hydrobromides of esters of the corresponding α-bromo-β-alkylaminopropionic acids (III, a-b) together with the hydrobromides of the original amines.



where a, R = $COOCH_3$, R' = H, R" = CH_3; b, R = $COOCH_3$, R' = H, R" = $CH_2C_6H_5$; c, R = $COOCH_3$, R' R" = $(CH_2)_5$; d, R = $COOCH_3$, R' = H, R" = C_6H_{11}; e, R = $COOCH_3$, R' = H, R" = $CH(CH_3)_2$; f, R = $COOCH_3$, R' R" = $(C_2H_4)_2O$; g, R = $COOCH_3$, R' = R" = C_2H_5; h, R = $COOCH_3$, R' = R" = CH_3; i, R = $COOCH_3$, R' R" = $(CH_2)_2$; j, R = CN, R' = H, R" = C_6H_{11}; k, R = CN, R' = H, R" = $CH_2C_6H_5$; l, R = CN, R' R" = $(CH_2)_5$.

According to the above reaction scheme we should also expect formation of one of the two possible compounds (IV) or (V), but these substances could not be isolated. Intermediate compounds of the type of (II) have not been isolated, either.

In the present work we continued the investigations of this reaction. The starting amines were cyclohexylamine, isopropylamine, aniline, dimethylamine, diethylamine, morpholine, and ethyleneimine. The derivatives of α-bromoacrylic acid were its methyl ester (I, R = $COOCH_3$) and nitrile (I, R = CN).

As in the preceding experiments [1], it was found that primary amines (cyclohexylamine and isopropylamine) very easily form compounds (III, d, e) whereas secondary amines (morpholine and diethylamine) only react under more drastic conditions. Reaction of α-bromoacrylonitrile (I, R = CN) with cyclohexylamine, benzylamine, and piperidine goes with rather more difficulty than the interaction of the α-bromoacrylate with the same amines. In these cases again we isolated the hydrobromides of nitriles of α-bromo-β-alkylaminopropionic acids (III, j-l). Cyclohexlamino- and benzylamino derivatives of these nitriles were found to be identical with compounds previously obtained by one of us [2] by the action of HBr on N-cyclohexyl- and N-benzylcyanoethyleneimines.

* See [1] for Communication I.

Ethyleneimine, dimethylamine, and aniline behave differently in reaction with methyl α-bromoacrylate (I, R = $COOCH_3$). Ethyleneimine relatively easily adds on at the double bond of the bromoacrylate, but in this case a compound of type (III) was not subsequently formed, nor was entry into the molecule of a second ethyleneimino group observed when ethyleneimine was used in excess. Accompanying the methyl ester of α-bromo-β-ethyleneiminopropionic acid (II, i) was a viscous oil which decomposed violently when its distillation in vacuo was attempted.

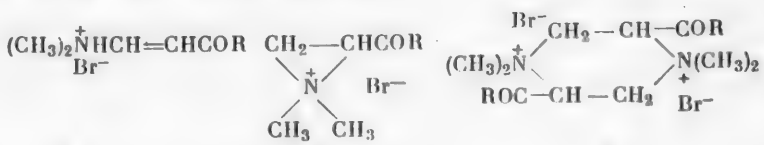
Treatment of (II, i) with HBr led, as was to be expected, to opening of the ethyleneimine ring with formation of the hydrobromide of β-carbomethoxy-β,β'-dibromodiethylamine (VI).

$$[BrCH_2CH_2NH_2CH_2CHBrCOOCH_3]^+Br^-$$
(VI)

Reaction of ester (I, R = $COOCH_3$) with dimethylamine gave (in addition to dimethylamine hydrobromide) a substance with the simplest empirical formula of $C_7H_{15}ON_2Br$ (VII), m. p. 111-112°. Its structure will be considered below.

Reaction with aniline under ordinary conditions results in isolation of only a little aniline hydrobromide. Reaction at 120° gave (in addition to a considerable amount of aniline hydrobromide) about 4% of methyl α, β-dianilinopropionate. The same compound is formed in 36% yield by the action of 3 moles aniline on one mole ester (I, R = $COOCH_3$), under conditions similar to those for the preparation of α,β-dianilino-β-phenylpropionic acid, described by Moureu and co-workers [3] (120°, 2 hr).

Since the product of condensation of α-bromoacrylic ester (I, R = $COOCH_3$) with ethyleneimine was compound (II, i), it seemed likely that analogous compounds could be obtained in other cases. Reaction with piperidine, diethylamine and dimethylamine under milder conditions actually gave compounds (II, c, g, h). Such compounds could not be isolated with primary amines due to the very great ease with which they changed into compounds of the type of (III). The methyl esters of α-bromo-β-piperidino-, diethylamino-, and dimethylaminopropionic acids (II, c, g, h) proved to be extremely unstable liquids, undergoing change after keeping for only 30-60 minutes. It was shown that (II, c) and (II, g) are also converted, under conditions similar to those employed in the reaction of methyl α-bromoacrylate with amines, into compounds (III, c, g). The latter are accompanied by the hydrobromides of the corresponding amines. A substance $C_8H_{12}O_2NBr$ (VIII) with m. p. 173-173.5° was obtained, however, from (II, h), together with the hydrobromide of dimethylamine. On comparing the empirical formulas of (VII) and (VIII), we see that the latter contains a $N(CH_3)_2$ group in place of the OCH_3 group. It was shown that the bromine atom in compounds (VII) and (VIII) is ionic. These compounds can therefore be represented by one of the following three structural formulas:



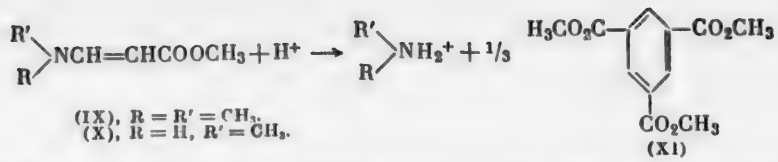
A B C

where for (VII) R = $N(CH_3)_2$, and for (VIII) R = OCH_3

Formula A must be rejected since compound (VIII) virtually does not react with $KMnO_4$ solution and does not exhibit a maximum in the UV spectrum.

A final choice between Formulas B and C necessitated further investigations.

As already pointed out in the previous communication [1], the formation of substances of the type of (V) as secondary products of disporportionation seemed to us more probable, since the reaction also goes with secondary amines when the formation of esters of the type of (IV) is impossible. It was therefore of interest to synthesize some esters of β-aminoacrylic acids of the type of (V) and to study their behavior towards proton-donating agents. With this objective we prepared the methyl esters of β-dimethylamino- (IX) and β-methylamino- (X) acrylic acids. It was found that treatment with dry HBr, and even with picric acid in benzene solution, converted compounds (IX) and (X) into hydrobromides or picrates of dimethylamine and methylamine, and the trimethyl ester of trimesic acid (XI).



(IX), R = R′ = CH_3.
(X), R = H, R′ = CH_3.

(XI)

It should be noted that the literature [4] reports the formation of aniline hydrochloride when dry HCl acts on β-anilinoacrylic ester. An amorphous yellow substance was also isolated; its structure was not established.

It may be thought that this transformation takes place under the catalytic influence of traces of water with intermediate formation of formylacetic ester, which is known to readily polymerize to the trimethyl ester of trimesic acid (XI). This theory is supported by the result of treatment of (IX) with aqueous hydrobromic acid. An oil is isolated which gives a positive silver-mirror reaction and is converted to (XI) on attempted distillation.

TABLE 1

$HBr \cdot RCH_2CHBrCOOCH_3$ (III, d-g)

R	Yield (%)	Crystallization from mixture of	Melting point*	Found (%) **				Calculated (%)			
				C	H	N	Br	C	H	N	Br
$C_6H_{11}NH$ (d)	42	EtOH and hexane (1:3)	141.7—142.7°	34.81	5.45	4.18	46.35	34.80	5.55	4.03	46.31
$(CH_3)_2CHNH$ (e)	49	EtAc and EtOH (10:1)	141.5—142.0	27.61	4.97	4.47	52.51	27.56	4.96	4.59	52.40
$(C_2H_5)_2N$ (f)	24.8	EtOH and hexane (1:3)	136.5—137.5	30.07	5.60	5.04	50.22	30.11	5.34	4.38	50.09
$O(C_2H_4)_2N$ (g)	64	EtOH and hexane (3:1)	167—167.5	28.83	4.70	4.03	48.13	28.82	4.53	4.21	47.99

* All of the compounds melted with decomposition.

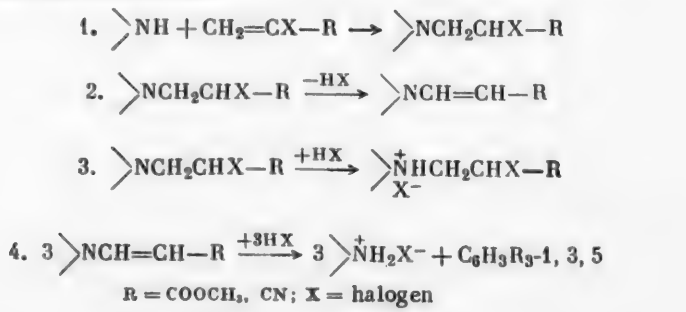
** Analyses were carried out in the analytical laboratory of the institute.

The properties of substances of the type of (V) may account for our failure to isolate them after reaction of ester (I, R = $COOCH_3$) with amines; they also fully explain our observation of the formation (in all of the cases) of considerable quantities of the hydrobromides of the original amines.

Direct proof of the formation of esters of β-alkylaminoacrylic acids during this reaction would be the isolation of the trimesic ester (XI) after reaction of ester (I, R = $COOCH_3$) with amines. Experiments were continued in this direction.

The instability of the β-dimethylaminoacrylic ester (IX) is also an additional reason for rejecting Formula A for compounds (VII) and (VIII).

On the basis of the foregoing data we can put forward as a working hypothesis the following mechanism of the reaction of type (I) compounds with amines.



R = $COOCH_3$, CN; X = halogen

Here R = $COOCH_3$ or CN, and X = halogen.

The ratio of reaction products will obviously depend on the proton-binding ability of the intermediate products, i.e., on their basicity, and the latter will also determine the rate of dehydrobromination of (II). Such a mechanism is more probable for secondary amines, but reaction of primary amines in similar fashion is not excluded.

EXPERIMENTAL

1. Hydrobromides of methyl esters of α-bromo-β-alkylaminopropionic acids (III, d-g). 0.02 mole methyl α-bromoacrylate (I, R = $COOCH_3$) was dissolved in 20 ml dry ether (or in ethyl acetate in the case of condensation with diethylamine), and a solution of 0.02 mole amine in 10 ml of the same solvent was introduced dropwise over 15-20 min at 15-20°. The mixture was stirred one hr and the precipitate of amine hydrobromide was filtered off (yield 5-17% calculated on the bromine). The filtrate was evaporated in vacuo and the residue heated for 10 min on a water bath (bath temperature 45-50°). The solidified mass was dissolved in chloroform and filtered; the solution was evaporated. The residue was triturated with ether, filtered, and recrystallized. In the case of condensation with diethylamine, the ethyl acetate solution was boiled for 1.5 hr on a water bath after the amine had been added, and then filtered; the filtrate was evaporated; the residue was stirred with ether, filtered and recrystallized. In the reaction with morpholine, the residue after removal of ether was dissolved in benzene and boiled for 3 hr. The mixture was then cooled and left at room temperature for 24 hr. The precipitated product was collected. Yields, constants and analyses of the prepared compounds are presented in Table 1.

2. Hydrobromides of α-bromo-β-alkylaminopropionitriles (III, j-l) were prepared in similar fashion to the esters (III, d-g) from α-bromoacrylonitrile (I, R = CN) and amines. The oils remaining after evaporation of the ether were dissolved in dry benzene and boiled. After cooling, the resulting crystals were filtered and recrystallized from a mixture of alcohol and hexane. Heating periods, yields, and melting points of the prepared compounds are given in Table 2.

TABLE 2

$HBr \cdot RCH_2CHBrCN$ (III, j-l)

R	Duration of heating in benzene	Yield (%)	Melting point
$C_6H_{11}NH$ * (j)	10 min	55	176—177°
$C_6H_5CH_2NH$ * (k)	2 hr	37.5	164.5—165.5
$(CH_2)_5N$ ** (l)	30 min followed by 48 hr at 20°	8	142—143

* Mixtures with specimens previously obtained [2] do not give a depression of melting point.

** Found %: C 32.55; H 4.54. $C_8H_{14}N_2Br_2$. Calculated %: C 32.23; H 4.73.

3. Methyl α-bromo-β-N-ethyleneiminopropionate (II, i). a) 5 g of α-bromoacrylate (I, R = $COOCH_3$) was dissolved in 20 ml dry ether, and 1.8 ml (10% excess) ethyleneimine in 10 ml ether was added. The mixture was stirred for 2 hr at 20°, the ether was evaporated in vacuo and the residue was distilled in vacuo. 2 g (32%) of compound was obtained; b. p. 102-108° (6 mm). 1.25 g of the original α-bromoacrylate was also recovered. The residue in the flask decomposed violently when the temperature of the bath was raised to above 170°. The main fraction was redistilled.

B. p. 104-105° (5 mm), n_D^{20} 1.4949, d_4^{20} 1.4797, MR_D 40.916; calc. 41.067.

Found %: C 34.57; H 4.82; N 6.73; Br 38.48. $C_6H_{10}O_2NBr$. Calculated %: C 34.60; H 4.84; N 6.87; Br 38.41.

b) The residue after evaporation of the ether (see a) was boiled in benzene for 3 hr; 1 g of an amorphous substance was collected; it dissolved in water and contained ionic bromine. The substance is evidently a polymer of ethyleneimmonium bromide [5]. After the polymer had been separated, the filtrate was fractionally distilled to give compound (II, i) in 40% yield.

c) 0.05 mole of methyl α,β-dibromopropionate and 0.11 mole of ethyleneimine were boiled in benzene solution in presence of 0.1 mole of triethylamine for 3 hr. Compound (II, i) was obtained in 30.5% yield.

4. Hydrobromide of β-carbomethoxy-β,β'-dibromodiethylamine (VI). 5.45 g of ethyleneimino ester (II, i) was dissolved in 30 ml dry ether and a stream of dry HBr was passed into the solution. The resulting precipitate was filtered and washed with ether to give 4.3 g (44.5%) of substance with m. p. 123-126°. It was recrystallized from a mixture of ethyl acetate and alcohol (10:1) and then from dioxane. Compound (VI) was obtained with m. p. 132-133° (decomp.); yield 3.0g (31%).

Found %: C 19.89; H 3.43; N 3.74; Br 64.75. $C_6H_{12}O_2NBr_3$. Calculated %: C 19.49; H 3.27; N 3.79; Br 64.81.

5. Condensation of α-bromoacrylate with dimethylamine. a) 5.4 g of α-bromoacrylate (I, R = $COOCH_3$) was dissolved in 30 ml of dry benzene and 1.82 g dimethylamine in 21 ml benzene was added dropwise. The mixture was stirred for 30 min and filtered from the precipitate of dimethylamine hydrobromide (0.3 g, m. p. 133°). The filtrate was boiled for 30 min and left overnight at room temperature. In the morning, 1.9 g of substance (VII) was filtered off; m. p. 111-112° (decomp.) (from ethyl acetate). For analysis the substance was recrystallized from acetone; m. p. 111.5-112.5° (decomp.).

Found %: C 35.27; H 6.67; N 12.00; Br^- 33.86. $C_7H_{15}ON_2Br$. Calculated %: C 35.20; H 6.32; N 11.71; Br^- 33.42.

Compound (VII) slowly decolorizes aqueous $KMnO_4$ solution. Evaporation of the filtrate from (VII) and distillation of the residue in vacuo gave 1.2 g of methyl α-bromo-β-dimethylaminopropionate (II, h) (constants in Table 3).

b) Boiling of 3.6 g of ester (I, R = $COOCH_3$) and 16 ml of benzene solution of dimethylamine for 2.5 hr gave 2.5 g of dimethylamine hydrobromide with m. p. 131-133° after recrystallization from a mixture of alcohol and hexane. From the filtrate was isolated a dark-colored oil which could not be purified.

TABLE 3

$RCH_2CHBrCOOCH_3$ (II, c, g, h)

R	Yield (%)	Boiling point (pressure in mm)	n_D	d_4	MR_D found	MR_D calc.
$CH_2(CH_2)_4N$ (c)	75	88—90° (1)	1.4918 (24°)	1.3079 (24°)	55.46	54.92
$(C_2H_5)_2N$ (g)	52	91—93 (9)	1.4665 (23°)	1.2546 (23°)	52.62	52.50
$(CH_3)_2N$ (h)	53	78 (9)	1.4659 (20°)	1.3300 (20°)	43.74	43.27

6. Condensation of α-bromoacrylate with aniline. a) 3.4 g of ester (I, R = $COOCH_3$) was mixed with 1.88 ml aniline and the mixture cautiously heated to 120° on an oil bath. The bath was removed and the mixture continued to boil for another 10 min. The mass was then cooled, 20 ml ether was added and the precipitate of aniline hydrobromide (2.2 g) was filtered off. The filtrate was evaporated in vacuo and the residue was distilled to give 1 g of the original bromoacrylate and 0.2 g of oil with b. p. 220-225° (6 mm). The oil was boiled for 2 hr with 5% alcoholic KOH solution. Dilution of the mixture with water followed by acidification led to separation of 0.1 g α,β-dianilinopropionic acid; m. p. 163.6-164.6° after two recrystallizations from alcohol.

Found %: C 69.90; H 6.42; N 10.87; $C_{15}H_{16}O_2N_2$. Calculated %: C 70.24; H 6.29; N 10.93.

b) Heating of 5.9 g aniline and 3.55 g bromoacrylate at 120° for 2 hr gave 2 g of methyl α,β-dianilinopropionate, saponification of which gave 1.5 g (36%) of the free acid.

7. Methyl esters of α-bromo-β-alkylaminopropionic acids (II, c, g, h). 0.04 mole bromoacrylate (I, R = = $COOCH_3$) in 10 ml ether was mixed with 0.04 mole amine in 10 ml ether; the mixture was stirred for one hr and filtered; the ether was taken off at reduced pressure and the residue distilled in vacuo. The products were colorless liquids decomposing after standing for 30-60 min. Yields and constants of the prepared esters are given in Table 3.

Treatment of esters (II, c, g) with dry HBr in ether gave their hydrobromides which proved identical with the corresponding hydrobromides synthesized by method 1.

The hydrobromide of the methyl ester of α-bromo-β-dimethylaminopropionic acid (III, h) was prepared from the corresponding ester (II, h) by the action of 25% HBr, followed by evaporation of the liquid and recrystallization of the solid from a mixture of methanol and ethyl acetate (1:6); m. p. 126-127° (decomp.), yield 83%.

Found %: C 24.68; H 4.46; N 4.82; Br 55.64. $C_6H_{13}O_2NBr_2$. Calculated %: C 24.76; H 4.50; N 4.81; Br 54.92.

The picrate of the methyl ester of α-bromo-β-dimethylaminopropionic acid melts at 133.5-134° (from 80% ethanol).

Found %: C 32.96; H 3.55; N 12.84; Br 18.42. $C_{12}H_{15}O_9N_4Br_2$. Calculated %: C 32.82; H 3.44; N 12.76; Br 18.20.

8. Disproportionation of methyl esters of α-bromo-β-alkylaminopropionic acids. a) 0.5 g of methyl α-bromo-β-piperidinopropionate (II, c) was boiled for 2 hr in benzene. Cooling, filtration, and recrystallization of the precipitate from a mixture of alcohol and ether gave 0.2 g of the hydrobromide of methyl α-bromo-β-piperidinopropionate (III, c) (m. p. of mixture with a previously prepared specimen [1] 154-155°) and 0.05 g of piperidine hydrobromide with m. p. 235°.

b) 0.7 g methyl α-bromo-β-diethylaminopropionate (II, g) was boiled in ethyl acetate for 3 hr. The mixture was left overnight and 0.05 g diethylamine hydrobromide (m. p. 213°) was collected by suction filtration. The filtrate was evaporated, and the residue (which solidified after standing in a refrigerator) was stirred with ether, filtered, and recrystallized from a mixture of alcohol and hexane. The yield of hydrobromide of methyl-α-bromo-β-diethylaminopropionate was 0.3 g; m. p. in admixture with a specimen obtained by method 1, 135-135.5°.

c) 1 g of methyl α-bromo-β-dimethylaminopropionate (II, h) was heated in 10 ml benzene for 30 min at 80° and then kept for 48 hr at 20°. There was obtained 0.4 g dimethylamine hydrobromide (m. p. 132°). The filtrate was evaporated and the residue worked up with alcohol to give 0.05 g of (VIII) with m. p. 172-173° (from aqueous alcohol). A solution of 2 g of ester (II, h) in 10 ml anhydrous alcohol was kept overnight at room temperature; crystals of (VIII) were deposited; yield 0.9 g; m. p. 173-173.5° (from 70% aqueous alcohol).

Found %: C 31.70; H 6.17; N 6.12; Br^- 35.12. $C_6H_{12}O_2NBr \cdot H_2O$. Calculated %: C 31.59; H 6.18; N 6.14; Br^- 35.04.

After 0.1278 g of the substance had been dried over P_2O_5 for 3 hr at 100°, the weight fell to 0.1174 g (calculated 0.1176 g). M. p. 172-172.5°.

Found %: Br^- 38.31; $C_6H_{12}O_2NBr$. Calculated %: Br^- 38.20.

9. Methyl β-dimethylaminoacrylate (IX). 4.65 g of methyl propionate was dissolved in 30 ml dry benzene, and 32 ml of a 7.92% solution of dimethylamine in benzene was added. The mixture was kept for 2 hr at room temperature and then the solvent was distilled off. Yield of substance with m. p. 46.5-48.5°, 6.25 g (88%). M. p. 48-49° after recrystallization from a mixture of benzene and hexane (1:8). B. p. 82-84° (1 mm).

Found %: C 55.87; H 8.63; N 10.60. $C_6H_{11}O_2N$. Calculated %: C 55.71; H 8.59; N 10.84.

10. Methyl β-methylaminoacrylate (X). Prepared by a method similar to that described for (IX), from 2.3 g methyl propionate and 15 ml of 6.3% methylamine (0.85 g CH_3NH_2) in benzene. Yield 1.5 g (47.5%).

B. p. 90-93° (8 mm), n_D^{24} 1.4412, d_4^{20} 1.0285; MR_D 29.57; calc. 30.08.
Found %: N 11.85. $C_5H_9O_2N$. Calculated %: N 12.16.

11. Trimethyl ester of trimesic acid (XI). a) 2.0 g of methyl β-dimethylaminoacrylate (IX) was dissolved in 20 ml anhydrous benzene and saturated with dry HBr. The solution was filtered and the precipitate dissolved in alcohol and reprecipitated with ether. The precipitate of dimethylamine hydrobromide was suction filtered. Weight 1.8 g (93%). The alcohol-ether filtrate was combined with the benzene filtrate and the solvents were taken off in vacuo. The residue of 1.2 g (85%) was crystallized from alcohol; m. p. 141-142°. Compound (XI) does not exhibit a melting point depression in admixture with a specimen prepared by the literature method [6].

Found %: C 56.90; H 5.04. $C_{12}H_{12}O_6$. Calculated %: C 57.13; H 4.80.

b) Treatment of 0.5g ester(IX) with 5 ml of 10% aqueous hydrobromic acid gave an oil which was extracted with ether. After removal of the ether, the residual oil gave a silver mirror. The substance decomposed during distillation and a small quantity of trimethyl trimesate (XI) with m. p. 141-142° sublimed.

c) 0.5 g ester (IX) was treated with a benzene solution of picric acid. Dimethylamine picrate was obtained (melting point and mixed melting point 157-158.5°) and 0.25 g of trimethyl trimesate (XI) was isolated from the filtrate; m. p. 141-142°.

(d) 0.5 g methyl β-dimethylaminoacrylate (X) was treated with dry HBr in ether solution. 0.4 g of methylamine hydrobromide was obtained with m. p. 249-250° and 0.3 g of trimethyl trimesate (XI) with m. p. 141-142°.

SUMMARY

1. Condensation of methyl α-bromoacrylate and of α-bromoacrylonitrile with primary and secondary amines gave hydrobromides of methyl esters of α-bromo-β-cyclohexylamino-, isopropylamino-, diethylamino-, -morpholinopropionic acids and the hydrobromides of the nitriles of α-bromo-β-benzylamino-, cyclohexylamino- and -piperidinopropionic acids.

2. Reaction of methyl α-bromoacrylate with ethyleneimine gave methyl α-bromo-β-ethyleneiminopropionate; reaction with aniline gave methyl α, β -dianilinopropionate; reaction with dimethylamine gave a compound $C_7H_{15}ON_2Br$ whose structure was not elucidated.

3. The intermediate products of reaction of secondary amines with methyl α-bromoacrylate were synthenesized (methyl esters of α-bromo-β-diethylamino- and -piperidinopropionic acid) and transformed into the hydrobromides of the methyl esters of α-bromo-β-alklaminopropionic acids. Under these conditions the methyl ester of α-bromo- β-dimethylaminopropionic acid was converted to a substance $C_6H_{12}O_2NBr$ whose structure could not be established.

4. The methyl esters of β-dimethylamino- and β-methylaminoacrylic acids were synthesized, and it was shown that proton-donating agents (HBr, picric acid) convert them into salts of the corresponding amines and trimethyl trimesate.

LITERATURE CITED

[1] V. K. Antonov, Zhur. Obshchei Khim. 29, 306 (1959).•

[2] V. K. Antonov, Zhur. Obshchei Khim. 29, 1132 (1959).•

[3] H. Moureu, P. Chovin, and L. Petit, Bull. Soc. Chim. 1573 (1955).

[4] F. Straus and W. Voss, Ber. 59, 1690 (1926).

[5] G. Jones, J. Org. Chem. 9, 125 (1944).

[6] H. Wislicenus and A. Bindemann, Liebigs Ann. 316, 42 (1901).

•Original Russian pagination. See C. B. translation.

THE SYNTHESIS OF 1,4-ENDOMETHYLENESPIRO-(5,5)-UNDECANE

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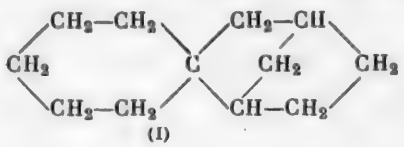
Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4011-4013,

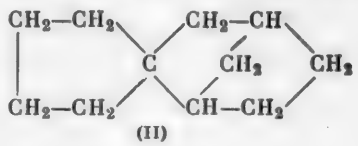
December, 1959

Original article submitted December 15, 1958

We previously described [1, 2] the synthesis of 1,4-endomethylenespiro-(5,5)-undecane (I) and 6,9-endomethylenespiro-(4,5)-decane (II) by dienic condensation of 2-methylenecyclohexanone-1 and 2-methylenecyclopentanone-1 with cyclopentadiene. The first step of the diene synthesis is formation of unsaturated tricyclic ketones—1,4-endomethylenespiro-(5,5)-undecen-2-one-7 in the first case, and 6,9-endomethylenespiro-(4,5)-decen-7-one-1 in the second case. The latter are then converted to spiran hydrocarbons by a series of steps.



(I)

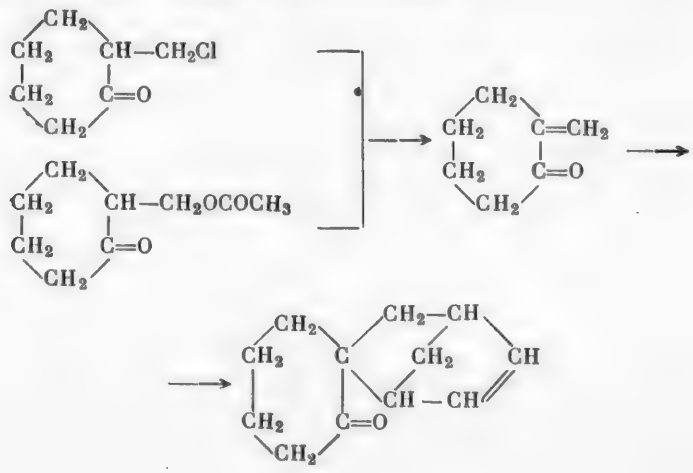


(II)

In the reaction with cyclopentadiene, we did not take the methyleneketones themselves but the corresponding Mannich bases—2-(N-dimethylaminomethyl)-cyclohexanone-1 and 2-(N-dimethylaminomethyl)-cyclopentanone-1. Decomposition of the latter during the reaction gives the methyleneketones and dimethylamine.

Arbuzov, Dyatkin, and Shevelev [3] showed that, in presence of potassium acetate, β-chloroketones can also enter into reaction with dienes. Examples are 1,4-dichlorobutanone-2 and 1-chloro-4-acetoxybutanone-2.

In the present work we made use of 2-(chloromethyl)-cyclohexanone-1 and 2-(acetoxymethyl)-cyclohexanone-1 as sources of 2-methylcyclohexanone-1. It was found that when heated in presence of potassium acetate, these compounds easily split off hydrochloric acid and acetic acid respectively and form 2-methylenecyclohexanone-1, which then enters into dienic synthesis with cyclopentadiene.



A particularly high yield of unsaturated tricyclic ketone (up to 77%) was obtained from the acetoxy derivative. The ketone was converted to the spiran hydrocarbon by the method previously described.

EXPERIMENTAL

2-Hydroxymethylcyclohexanone-1. A three-liter round-bottomed flask, fitted with stirrer and seal, dropping funnel, thermometer, and reflux condenser, was charged with 981 g of cyclohexanone, 200 g of 30% formaldehyde solution (d 1.092) and a few drops of bromothymol blue indicator. A 4% aqueous sodium hydroxide solution was slowly stirred into the reaction mixture from a dropping funnel until the liquid had a faint blue color. Stirring was continued for another 2.5 hr at 35°. To the flask was then added 10 g of hydroquinone, and the mixture stirred for another 30 min. The ether was distilled off from the ethereal extract (dried with anhydrous magnesium sulfate), and the residue was fractionated in vacuo to give 132.5 (51.7%) of 2-hydroxymethylcyclohexanone-1.

B. p. 83° (3 mm), n_D^{20} 1.4791, d_4^{20} 1.0713, MR_D 33.93. $C_7H_{12}O_2$. Calculated 33.86.
Literature data: b. p. 114-115° (16 mm) [4], b. p. 89-91° (5 mm), n_D^{25} 1.4766 [5]; b. p. 110-112° (12 mm), n_D^{11} 1.4790, d_4^{14} 1.070 [6].

2-Acetoxymethylcyclohexanone-1. a) 30.6 g of acetic anhydride, acidified with a drop of strong sulfuric acid, was put into a three-necked round-bottomed flask of 250 ml capacity, fitted with stirrer, dropping funnel, and reflux condenser (the latter topped by a calcium chloride tube). In the course of 20 min, 20 g of 2-hydroxymethylcyclohexanone-1 was added with stirring; the temperature rose to 40°. The mixture was then heated with stirring on a water bath for a further 1.5 hr at 40-41°. Fractionation in vacuo gave 14.6 g (55%) of 2-acetoxymethylcyclohexanone-1.

B. p. 101° (3 mm), n_D^{20} 1.4632, d_4^{20} 1.0787, MR_D 43.48; calc. 43.23.
Found %: C 63.80, 63.53; H 8.29, 8.07. $C_9H_{14}O_3$. Calculated %: C 63.51; H 8.29.

b) In the same apparatus was placed 10 g of 2-hydroxymethylcyclohexanone-1 and 45 ml of anhydrous pyridine. Acetic anhydride (15.9 g) was then slowly added at such a rate that the temperature remained at 20°. The mixture was then heated for 1.5 hr on a water bath at 48-50° and poured into ice water; the oily layer was collected; the aqueous layer was extracted with ether and the extract combined with the oil. The latter was washed in succession with 2 N hydrochloric acid, 5% bicarbonate solution, and water; it was then dried with anhydrous sodium sulfate, the ether was distilled off and the residue distilled in vacuo to give 7.2 g (54.2%) of 2-acetoxymethylcyclohexanone-1.

B. p. 104° (3 mm), n_D^{20} 1.4639, d_4^{20} 1.0780, MR_D 43.56; calc. 43.23.

2-Chloromethylcyclohexanone-1. Absolute ether (100 g) was saturated at −5° with a stream of dry hydrogen chloride until the increase in weight was 18 g. From a dropping funnel 20 g of 2-hydroxymethylcyclohexanone-1 was added with vigorous stirring at −3°. After being stirred for one hr at −3° and stood for four hr at room temperature, the mixture was poured onto crushed ice. The oily layer was collected and combined with the ethereal extract of the aqueous layer. Washing with saturated bicarbonate solution and drying with anhydrous magnesium sulfate was followed by removal of the ether in the cold in a low vacuum. The residual viscous, pale-yellow oil (19.5 g) was fractionated under low pressure in a nitrogen atmosphere (risk of resinification). There was obtained 3.2 g of 2-chloromethylcyclohexanone (14%) with b. p. 66-68° (15 mm), n_D^{20} 1.4801. A colorless liquid with a pungent odor, rapidly resinifying on standing.

1,4-Endomethylenespiro-(5,5)-undecen-2-one-7. a) Reaction of cyclopentadiene with 2-acetoxymethylcyclohexanone-1. In a 100 ml round-bottomed flask fitted with reflux condenser (topped by a calcium chloride tube) were placed 17 g of 2-acetoxymethylcyclohexanone-1, 13.2 g cyclopentadiene, 0.1 g of anhydrous potassium acetate, and a small pinch of hydroquinone. The mixture was heated at the boil on a water bath for four hr, dissolved in ether, and washed with water and sodium bicarbonate solution. After drying with magnesium sulfate, the ether was driven off and the residue fractionated in vacuo to give 13.6 g (77.3%) of 1,4-endomethylenespiro-(5,5)-undecen-2-one-7.

B. p. 97° (1 mm), n_D^{20} 1.5153, d_4^{20} 1.0571, MR_D 50.29. $C_{12}H_{16}O$. Calculated 50.56.
Literature data: b. p. 107-107.5° (4 mm), n_D^{20} 1.5154, d_4^{20} 1.0591 [1].

Semicarbazone: m. p. 196-197°.

b) Reaction of cylcopentadiene with 2-chloromethylcyclohexanone. In the same apparatus 19 g of 2-chloromethylcyclohexanone-1, 17.2 g of cyclopentadiene, 80 ml ethyl alcohol, 13.7 g of anhydrous potassium acetate, and a small pinch of hydroquinone were heated for 2.5 hr at the boiling point of the mixture. The precipitate of potassium chloride was filtered and washed with alcohol. The alcoholic solutions were combined and the alcohol distilled off in a low vacuum. The residue was dissolved in ether. After the usual working-up of the ethereal solution, the ether was driven off and the residue fractionated in vacuo to give 9 g (39.3%) of 1,4-endomethylenespiro-(5,5)-undecen-2-one-7.

B. p. 101° (2 mm), n_D^{20} 1.5151, d_4^{20} 1.0576, MR_D 50.52. $C_{12}H_{16}OF$. Calculated 50.56.

The 1,4-endomethylenespiro-(5,5)-undecen-2-one-7 was subsequently transformed into 1,4-endomethylenespiro-(5,5)-undecane in the manner previously described [1].

Constants of the hydrocarbon:

B. p. 98° (12 mm), setting point −35.4°,* n_D^{20} 1.4991, d_4^{20} 0.9471, MR_D 50.94. $C_{12}H_{20}$. Calculated 51.01.

The constants are extremely close to those previously reported [1].

SUMMARY

1,4-Endomethylenespiro-(5,5)-undecane can be prepared by dienic condensation of cyclopentadiene with 2-acetoxymethylcyclohexanone-1 or 2-chloromethylcyclohexanone-1.

LITERATURE CITED

[1] N. V. Elagina, V. M. Brusnikina, and B. A. Kazanskii, Doklady Akad. Nauk SSSR 106, 1015 (1956).••

[2] N. V. Elagina, T. V. Stabnikova, and B. A. Kazanskii, Doklady Akad. Nauk SSSR 124, 1243 (1959).••

[3] Yu. A. Arbuzov, B. L. Dyatkin, and S. A. Shevelev, Doklady Akad. Nauk SSSR 112, 261 (1957).••

[4] C. Mannich and W. Brose, Ber. 56, 833 (1923).

[5] H. Zi, J. Am. Chem. Soc. 76, 2289 (1954).

[6] J. Colonge, J. Dreux, and H. Delplace, Bull. Soc. Chim. 1635 (1956).

• Determined in the laboratory of chemical thermodynamics of the Moscow State University.

•• Original Russian pagination. See C. B. translation.

ACID-CATALYZED SYNTHESIS OF ESTERS AND OTHER CARBOXYLIC ACID DERIVATIVES FROM CARBON MONOXIDE, OLEFINS, AND ACYLATING COMPOUNDS

III. SYNTHESIS OF ESTERS FROM NORMAL C_5-C_7 α-OLEFINS

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4014-4018,

December, 1959

Original article submitted December 29, 1958

We previously [1] submitted details of a new two-stage synthesis of carboxylic acid esters from carbon monoxide, olefins, and alcohols and of the mechanism of this process. The catalyst was concentrated sulfuric acid, which forms intermediate acylsulfuric acids with carbon monoxide and olefins. The main reaction products obtained by this method [2] were esters of trimethylacetic acid from isobutene and esters of α-methylbutyric acid from n-butene.

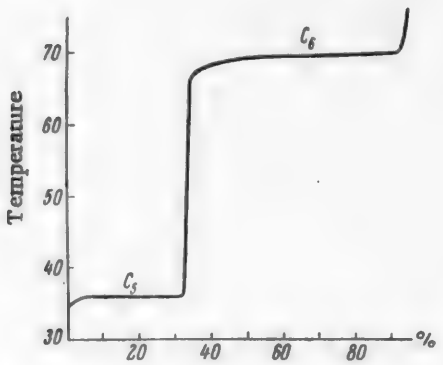

Fig. 1. Fractionation curve of hydrogenated C_5-C_8 synthin fraction.

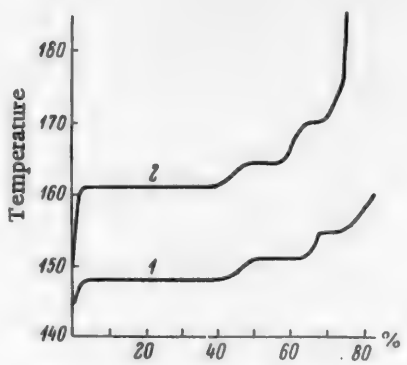

Fig. 2. Fractionation curves of mixtures of esters obtained from 1-hexene. 1) Methyl esters; 2) ethyl esters.

In the present paper we submit the results of experiments on carbalkoxylation of C_5-C_7 α-olefins by this method. The first reaction step—interaction of olefin, CO, and H_2SO_4—proceeded at 20-40° and an initial CO pressure of 80 atm; in the second step methyl or ethyl alcohol was added to the reaction mixture and the corresponding esters were formed. The first step was conducted in a stainless steel autoclave fitted with a turbine stirrer with a speed of 800 rpm and a dropping tube for the liquid olefin. The procedure for synthesis under pressure has been described [2]. The resulting ester mixtures were distilled from a Favorskii flask in vacuo (3 mm) and then precision-fractionated in a 90-plate column. Fractions corresponding to individual esters were converted

to the corresponding acid anilides [2] which were recrystallized from alcohol to constant melting points. These melting points served to identify the original esters. Mixtures of anilides prepared from methyl and ethyl esters of a given acid did not exhibit any depression of melting point.

The yields of esters obtained by carbalkoxylation of olefins were 65-100% on the CO absorbed and 55-75% on the original olefin. The main reaction product was always an ester of a carboxylic acid with one carbon atom more than the original olefin and with two methyl radicals at the carbon atom adjacent to the carboxyl group. A second product (in much lower yield) was an ester of an acid with the same number of carbon atoms with an ethyl radical at the carbon atom adjacent to the carboxyl group. The following methyl or ethyl esters were identified in the products from C_5-C_7 olefins: From 1-hexene, α,α-dimethylvaleric (36-42%) and α-ethylvaleric (5%); from 1-heptene, α,α-dimethylcaproic (55-64%) and α-ethylcaproic (5%); from 1-pentene (synthin fraction) α,α-dimethylbutyric and α-ethylbutyric in 2:1 ratio. The data show that during the reaction, the olefin undergoes skeletal isomerization as the main step and double-bond shift (or hydrogen migration) as the secondary step. It may be suggested that these transformations proceed with intermediate development of carbonium ions. On this basis the formation of esters from 1-heptene can be represented by the following equations [1]:

$$CH_3(CH_2)_4CH{=}CH_2 + H_2SO_4 \longrightarrow CH_3(CH_2)_4\overset{+}{C}HCH_3 + \overset{-}{O}SO_3H \longrightarrow$$

$$\longrightarrow \begin{matrix} CH_3(CH_2)_3\overset{+}{C}HC_2H_5 \\ CH_3(CH_2)_3\overset{+}{C}(CH_3)_2 \end{matrix} + \overset{-}{O}SO_3H \xrightarrow{CO} \begin{matrix} CH_3(CH_2)_3CH(C_2H_5)\overset{+}{C}O \\ CH_3(CH_2)_3C(CH_3)_2\overset{+}{C}O \end{matrix} + \overset{-}{O}SO_3H \rightleftarrows$$

$$\rightleftarrows \begin{matrix} CH_3(CH_2)_3CH(C_2H_5)COOSO_3H \\ CH_3(CH_2)_3C(CH_3)_2COOSO_3H \end{matrix} \xrightarrow{ROH} \begin{matrix} CH_3(CH_2)_3CH(C_2H_5)COOR \\ CH_3(CH_2)_3C(CH_3)_2COOR \end{matrix} + H_2SO_4$$

EXPERIMENTAL

The 1-hexene (b. p. 63.4-64.0°, d_4^{20} 0.6732, n_D^{20} 1.3880, bromine number 189.1) and 1-heptene (b. p. 93.4-93.8°, d_4^{20} 0.6975, n_D^{20} 1.4000, bromine number 163.2) used in the work were synthesized respectively from hexyl alcohol (b. p. 157-158°, d_4^{20} 0.8183, n_D^{20} 1.4185) and heptyl alcohol (b.p. 176-177°, d_4^{20} 0.8222, n_D^{20} 1.4249). These alcohols were esterified with a mixture of acetic anhydride and acetyl chloride; the resulting acetates were decomposed at 460-490° over glass wool in a nitrogen stream [3]. The olefins prepared in this manner were suitably purified and then distilled in a 90-plate column. Another starting material for synthesis of esters was a 35-75° synthin fraction containing 39.6% of unsaturated hydrocarbons. As we see from the fractionation curve (Fig. 1), a part of this fraction after complete hydrogenation (over platinized carbon with addition of H_2PtCl_6) contained C_5 and C_6 normal hydrocarbons in a ratio of 1:2.

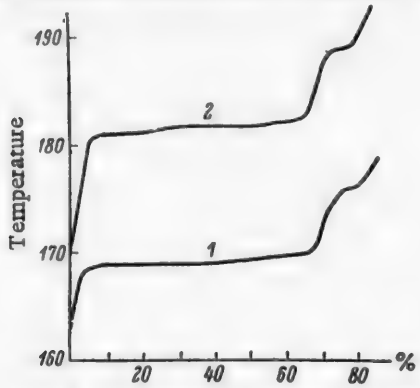

Fig. 3. Fractionation curves of mixtures of esters prepared from 1-heptene. 1) Methyl esters; 2) ethyl esters.

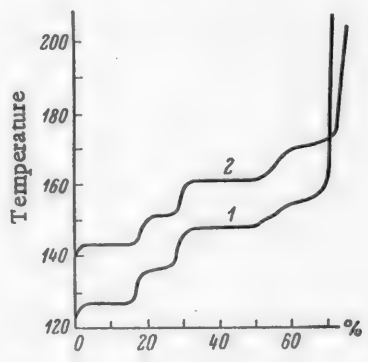

Fig. 4. Fractionation curves of mixtures of acids obtained from C_5-C_6 synthin fraction. 1) Methyl esters; 2) ethyl esters.

Operating conditions for all of the experiments on synthesis of esters and their results are presented in Table 1, fractionation curves of ester mixtures in Figs. 2-4, and constants of the fractions in Table 2. In each experiment the quantity of sulfuric acid (d 1.84) taken was 0.5 liter.

1-Hexene was transformed into a mixture of esters containing over 75% of esters of C_7 acids. As we see from Fig. 2 the main reaction products are esters of α,α-dimethylvaleric acid (40%, first plateau on curves of Fig. 2). There is a considerably smaller proportion of esters of α-ethylvaleric acid (third plateau on curves of Fig. 2).

TABLE 1

Synthesis of Esters from Normal C_5-C_7 α-Olefins

Expt. no.	Amount taken (in ml)		CO pressure (in atm)		CO absorbed		Ester yields		
	of liquid olefin	of alcohol	initial	final	in liters	in % of theory	in ml	in % of CO absorbed	in % of original olefin
1	C_5-C_6 synthin fraction (1500)	Methyl (800)	80	47	79.5	77.6	405	71.5	55.3
2	C_5-C_6 synthin fraction (1200)	Ethyl (800)	80	46	68.0	83.0	350	65.0	53.7
3	1-Hexene (214)	Methyl (210)	80	32	28.4	74.0	178	85.5	63.6
4	1-Hexene (214)	Ethyl (300)	80	31	29.0	75.4	205	87.2	66.2
5	1-Heptene (115)	Methyl (200)	80	56	14.2	77.5	113	100	76.2
6	1-Heptene (115)	Ethyl (250)	80	56	14.2	77.5	115	100	71.0

Literature data for methyl α,α-dimethylvalerate: b. p. 144-145° [4], melting point of anilide 73.5° [5]; for methyl α-ethylvalerate: b. p. 155-156.5°; ethyl ester of same acid: 169-171° [6].

We were unable to prepare an anilide with constant melting point from fractions (about 12%) corresponding to the second plateau on the curves of Fig. 2. This indicates the presence of mixtures—possibly of esters of α-methyl-α-ethylbutyric and α-ethyl-β-methylbutyric acids. According to [7] the boiling points of ethyl esters of these acids (166-166.5° and 164-165°, respectively) are close to the boiling points of the fractions in question.

1-Heptene was transformed into a mixture of esters containing about 80% of esters of C_8 acids. We see from Fig. 3 that the greater part (55-64%) of the reaction product consists of methyl or ethyl α,α-dimethylcaproate and a very much smaller proportion (5%) of the corresponding ester of α-ethylcaproic acid.

Literature data: Methyl α,α-dimethylcaproate boils at 168.5°, d_4^{25} 0.8707, n_D^{25} 1.4124 [8]; the anilide melts at 88° [9]; methyl α-ethylcaproate has b. p. 176° [10], d_4^{20} 0.8731, n_D^{20} 1.4142 [11]; ethyl ester: b. p. 189-191°, d_4^{20} 0.8628 [12], 0.8619 [13], n_D^{20} 1.4128 [12], n_D^{18} 1.4189 [13]; the anilide melts at 88-89° [14].

The melting points that we found for these anilides are very similar (88 and 86°); but their mixture melts at 76°, proving conclusively that the original substances were derivatives of different acids.

The synthin fraction with b. p. 35-75° (containing normal pentenes and normal hexenes in 1:2 ratio) gave mixtures of methyl and ethyl esters in which esters of the following acids were identified (Table 2): α,α-dimethylbutyric (12-14%), α-ethylbutyric (7%), α,α-dimethylvaleric (17-18%) and α-ethylvaleric (8%). Four plateaus on the curves of Fig. 4 correspond to these esters. On the basis of the results obtained when starting from 1-hexene, we can conclude that the first two esters were derived from n-pentene and the second two from n-hexene present in the original synthin fraction.

Literature data: Methyl α,α-dimethylbutyrate boils at 125-125.5° (746 mm), d_4^{25} 0.8943, n_D^{25} 1.3991; the ethyl ester boils at 142.8-143.2° (740 mm) [15], 141.8-142.2° (746 mm) [16], d_4^{25} 0.8601, n_D^{20} 1.3989 [14], 1.4024 [15]; the anilide melts at 90.5-91° [9], 91-92° [17], 91.4° [18]; methyl α-ethylbutyrate boils at 135-137° (736 mm), $d_4^{12.5}$ (0.8886, $n_D^{12.5}$ 1.40669 [19]; the ethyl ester boils at 151° (751.4 mm), d_0^{18} 0.8686 [20]; the anilide melts at 124.3-124.5° [21].

TABLE 2

Esters Prepared from C_5-C_7 Olefins, Carbon Monoxide, and Methyl and Ethyl Alcohols

Starting olefin	Acid component of ester	Boiling range (at 760 mm)	d_4^{20}	n_D^{20}	Melting point of anilide
Methyl esters					
C_5-C_6 synthin fraction	α,α-Dimethylbutyric	127.1–127.3°	0.8817	1.4019	92°
	α-Ethylbutyric	135.1–137.2	0.8795	1.4020	125
	α,α-Dimethylvaleric	147.4–148.0	0.8762	1.4083	74
	α-Ethylvaleric	150.1–154.8	0.8803	1.4100	90
1-Hexene	α,α-Dimethylvaleric	147.4–148.5	0.8758	1.4082	74
	α-Ethylvaleric	154.4–154.8	0.8752	1.4082	90
1-Heptene	α,α-Dimethylcaproic	168.6–169.8	0.8762	1.4150	88
	α-Ethylcaproic	176.2–176.4	0.8719	1.4140	86
Ethyl esters					
C_5-C_6 synthin fraction	α,α-Dimethylbutyric	143.1–143.4	0.8642	1.4022	92
	α-Ethylbutyric	150.7–152.0	0.8654	1.4038	125
	α,α-Dimethylvaleric	160.4–161.0	0.8603	1.4075	74
	α-Ethylvaleric	169.0–170.9	0.8635	1.4098	90
1-Hexene	α,α-Dimethylvaleric	161.0–161.5	0.8607	1.4075	74
	α-Ethylvaleric	169.3–171.0	0.8649	1.4096	90
1-Heptene	α,α-Dimethylcaproic	181.1–182.4	0.8646	1.4144	88
	α-Ethylcaproic	189.0–189.7	0.8621	1.4143	86

SUMMARY

1. Reaction between C_5-C_7 normal α-olefins, carbon monoxide, and methyl or ethyl alcohol, at 20-40° and 80 atm, in presence of sulfuric acid gave esters of carboxylic acids in a yield of 55-75% on the original olefin and 70-100% on the carbon monoxide.

2. The main products of the reaction were esters of α,α-dimethyl- and α-ethylalkanic acids containing one carbon atom more than the original olefin.

LITERATURE CITED

[1] Ya. T. Éidus, K. V. Puzitskii, and K. G. Ryabova, Doklady Akad. Nauk SSSR 120, 323 (1958); Author's certif. 114673 (1958).

[2] K. V. Puzitskii, Ya. T. Éidus, K. G. Ryabova, and I. V. Guseva, Zhur. Obshchei Khim. 29, 9 (1959).*

[3] J. van Pelt and J. P. Wibaut, Rec. trav. chim. 60, 55 (1941).

[4] R. Locquin and L. Leers, Bull. Soc. Chim. (4) 39, 434 (1926).

[5] D. V. N. Hardy, J. Chem. Soc. 468 (1938).

[6] P. Rasetti, Bull. Soc. Chim. (3) 33, 686 (1905).

* Original Russian pagination. See C. B. Translation.

[7] A. W. Crossley and H.R. LeSueur, Proc. Chem. Soc. 15, 225 (1900); J. Chem. Soc. 77, 93 (1900); A. A. Sacks and J. G. Aston, J. Am. Chem. Soc. 73, 3902 (1951).

[8] S. M. McElvain and C. L. Aldridge, J. Am. Chem. Soc. 75, 3993 (1953).

[9] D. D. Coffman and J. R. Roland, J. Am. Chem. Soc. 72, 3393 (1950).

[10] K. E. Schulte, H. Krause, and J. Kirschner, Hoppe-Seylers Z. physiol. Chem. 287, 239 (1951).

[11] A. D. Petrov, V. M. Melekhin, and O. M. Pefedov, Izvestiya Akad. Nauk SSSR, Otdel. Khim. Nauk 580 (1955).•

[12] P. A. Levene and F. A. Taylor, J. Biol. Chem. 54, 354 (1922).

[13] M. Häusermann, Helv. Chim. Acta 34, 2172 (1951).

[14] G. S. Skinner and J. F. Perkins, J. Am. Chem. Soc. 72, 5569 (1950).

[15] H. C. Brawn and R. B. Kornblum, J. Am. Chem. Soc. 76, 4510 (1954).

[16] B. B. Corson, J. S. Thomas, and D. D. Waugh, J. Am. Chem. Soc. 51, 1951 (1929).

[17] A. Quilico, Gazz. 78, 111 (1948).

[18] M. Hommelen, Bull. Soc. Chim. Belg. 42, 213 (1933).

[19] V. Grignard, Ann. Chim. (7) 27, 568 (1902).

[20] A. Zaizev, Liebigs Ann. 143, 352 (1878).

[21] J. M. Holbert, J. Am. Pharm. Assoc., Sci. Ed. 35, 315 (1946); C. A. 41, 2861 (1947).

A NEW METHOD OF SYNTHESIS OF ESTERS OF PHOSPHINIC AND THIOPHOSPHINIC ACIDS

XXXIII. REACTIONS OF PARTIAL ESTERS OF PHOSPHINOUS ACIDS WITH KETENE

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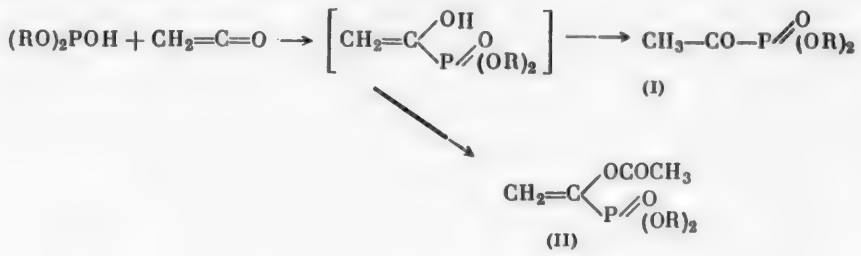
Translated from Zhurnal Obshchei Khimii, Vol. 29, No. pp. 4019-4021,

December, 1959

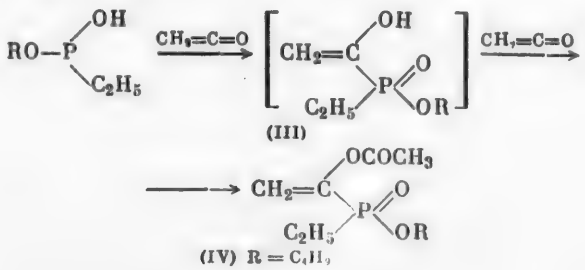
Original article submitted December 22, 1958

In the preceding paper [1] we reported on the addition to ketene of a series of dialkylphosphorous and dialkylthiophosphorous acids. Reaction of ketene with dimethyl-, diethyl-, and dibutylphosphorous acids gave two products in each case: dialkyl esters of acetophosphinic acid and products of their further reaction with ketene. Product (I) was formed in considerably larger quantity than (II).



Acetothiophosphinic esters could not be isolated after reaction of dialkylthiophosphorous acids with ketene. These esters are apparently more reactive than acetophosphinic esters and enter completely into reaction with ketene to form esters of α-acetoxyvinylphosphinic acids. Analogous results have been reported [2, 3] for reaction of dialkylphosphorous acids with ketene.

In the further course of the work, we studied the interaction of partial esters of ethyl- and phenylphosphinous acids with ketene. Reactions were carried out in a solvent in absence of catalyst. Reaction of ketene with ethyl and butyl esters of ethylphosphinous acid gave mainly esters of α-acetoxyvinylethylphosphinic acid. Esters of acetoethylphosphinic acid were isolated in small quantity. The latter could not be detected if ketene was passed into the reaction mixture for a long period.



That the reaction goes via product (III) as intermediate was proved by treating the butyl ester of acetoethylphosphinic acid with ketene. The result was formation of the butyl ester of α-acetoxyvinylethylphosphinic acid (IV).

Ozonolysis of the ethyl ester of acetoxyvinylethylphosphinic acid yielded formaldehyde, which was identified as the product of condensation with dimedon.

The prepared products are colorless and have a pleasant odor.

The yield of acetophenylphosphinic esters was higher than that of acetoxyvinylphosphinic esters when ketene was reacted with esters of phenylphosphinous acid. Short-period passage of ketene through the n-propyl ester of phenylphosphinous acid gave only the n-propyl ester of acetophenylphosphinic acid.

The results show that esters of acetophenylphosphinic acids react very much more slowly with ketene than esters of acetophosphinic acids and especially esters of acetothiophosphinic acids.

TABLE

Prep. no.	Formula	Boiling point at 10 mm	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	% P found	% P calc.	Yield (in %)
1	$CH_3=C(OCOCH_3)-P(=O)(C_2H_5)-OC_2H_5$	127°	1.4510	1.1010	50.39	49.55	14.73	15.03	30
2	$CH_3-C(=O)-P(C_2H_5)(=O)-OC_4H_9$	134—136	1.4471	1.0598	48.38	48.379	15.7	16.13	30
3	$CH_3=C(OCOCH_3)-P(C_2H_5)(=O)-OC_4H_9$	145—146	1.4512	1.0737	58.72	58.79	12.83	13.25	53
4	$CH_3-C(=O)-P(C_6H_5)(=O)-OCH_3$	142—143	1.4891	1.1698	48.88	49.32	15.2	15.65	36
5	$CH_3=C(OCOCH_3)-P(C_6H_5)(=O)-OCH_3$	165—166	1.5001	1.1802	59.84	59.72	12.4	12.89	6
6	$CH_3-C(=O)-P(C_6H_5)(=O)-OC_2H_5$	146—147	1.4968	1.1376	54.44	54.014	14.21	14.6	30
7	$CH_3=C(OCOCH_3)-P(C_6H_5)(=O)-OC_2H_5$	172—173	1.5078	1.1621	65.16	64.33	11.63	12.19	15
8	$CH_3-C(=O)-P(C_6H_5)(=O)-OC_2H_5$	155	1.5028	1.1095	58.91	58.63	13.22	13.69	53

EXPERIMENTAL

Procedure for addition of partial esters of phosphinous acids to ketene. Ketene was prepared with a ketene lamp with an output of 0.05 mole per hr. After passage through water condensers, the ketene entered a reaction flask fitted with condenser and thermometer. Reactions were carried out with 10-20 g of esters of ethyl- or phenylphosphorous acids, 50-75 ml of dioxane and an excess of ketene. The reaction mixture was held at a temperature of 35-45°. Solvent was removed from the reaction mixture by distillation in vacuo, and the residue was distilled from an Arbuzov flask. The products were redistilled several times from small columns.

Constants of the preparations, analyses (phosphorus), molar refractions and yields are set forth in the table.

Ozonolysis of ether ester of α-acetoxyvinylethylphosphinic acid. Ozonized oxygen was passed for 18 hr through a solution of 2 g of the ethyl ester of acetoxyvinylethylphosphinic acid in 20 ml of carbon tetrachloride

with ice-water cooling. After the carbon tetrachloride had been distilled off in vacuo, the ozonides were decomposed by heating with water. Formaldehyde was detected in the first 20 ml of distillate in the form of the dimedon condensation product. Colorless acicular crystals were obtained with m. p. 189-190° (mixed melting test gave m. p. 189°).

Reaction of n-butyl ester of acetoethylphosphinic acid with ketene. Ketene was passed for 6 hr into a solution of 6.5 g of n-butyl ester of acetoethylphosphinic acid in 30 ml of dioxane. The temperature of the reaction mixture was held at about 30-35°. The dioxane was taken off in vacuo and the residue distilled from an Arbuzov flask. Several fractionations gave 3.8 g of the n-butyl ester of acetoxyvinylphosphinic acid with b. p. 145-146° (10 mm), n_D^{20} 1.4512, d_4^{20} 1.0737.

SUMMARY

1. A study was made of the addition to ketene of the ethyl and butyl esters of the ethylphosphorous acid and of the methyl, ethyl, and propyl esters of phenylphosphorous acid.

2. The reaction goes in two steps. The initially formed esters of acetoethylphosphinic and acetophenylphosphinic acids react further with ketene to form esters of acetoxyvinylethylphosphinic and acetoxyvinylphenylphosphinic acids, respectively.

LITERATURE CITED

[1] V. I. Nikitina and A. N. Pudovik, Zhur. Obshchei Khim. 29, 1219 (1959).*

[2] I. Kennedy and Meaburn, C. A. 4933e (1957).

[3] McConnell and Coover, J. Org. Chem. 830 (1958).

*Original Russian pagination. See C. B. translation.

CYCLOALKYLATION OF PHENOLS AND THEIR ETHERS

II. CONDENSATION OF PHENOL WITH CYCLOPENTANOL

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4021-4024,

December, 1959

Original article submitted December 7, 1958

In preceding communications [1, 2] one of us showed the possibility of using cyclohexanol for alkylation of phenol and its ethers in presence of $AlCl_3$ and H_3PO_4. Very little work has been published on introduction of the cyclopentyl radical into the aromatic ring. More attention has been devoted to cyclopentylbenzene, which has been synthesized by various methods [3-7].

p-Cyclopentylphenol was first prepared [8] from 1,1-dihydroxydiphenylcyclopentane (the latter had been obtained by condensation of phenol with cyclohexanol in presence of hydrochloric acid). Other authors later condensed phenol [9] and aniline [10] with cyclopentanol in presence of aluminum chloride and also obtained p-cyclopentylphenol. Hoffman [11] isolated o- and p-cyclopentylphenols in presence of zinc chloride. Cyclopentenylphenols were synthesized [12] in presence of phosphoric acid and reduced to give both of the isomeric cyclopentylphenols.

We have studied the condensation of phenol with cyclopentanol in presence of aluminum chloride and phosphoric acid. Reaction components were used in various amounts and the order of addition of starting substances was varied. Condensation in presence of phosphoric acid was conducted with excess of the latter (3 moles) and with an equimolar alcohol: phenol ratio at 50-120° for 5-8 hr. Under optimum conditions (at 70°) the yield of monoalkyl products was 84%. Reaction products were separated into phenolic and nonphenolic components by treatment with 20% NaOH. From the phenolic portion were isolated crystalline p-cyclopentylphenol and liquid o-cyclopentylphenol.

In condensations in presence of aluminum chloride, the reactions were performed with excess of phenol (5 moles) and with equimolar quantities of cyclopentanol and aluminum chloride. The optimum conditions were addition of aluminum chloride to the mixture of phenol (excess) and alcohol at 20-30° in the course of 1-1.5 hr. The reaction mixture was thereupon heated at 50-150° for 5 hr. Under these conditions at 50° the yield of reaction products can reach 74%. If aluminum chloride is used, the subsequent working-up with 20% NaOH does not lead to formation of a solid phenate of para-isomer. Prior to the alkali treatment, the excess phenol must therefore be removed from the reaction mixture by distillation or by repeated washing with hot water. Subsequent treatment of the residue with 20% alkali leads to complete separation of o- from p-cyclopentylphenol. A small quantity of nonphenolic fraction with b.p. 110-150° (14 mm) was isolated in all experiments in presence of aluminum chloride and phosphoric acid.

One of the possible reaction products—cyclopentyl phenyl ether—isomerizes to o-cyclopentylphenol during distillation irrespective of whether the catalyst is $AlCl_3$ or H_3PO_4. This explains why it could only be isolated pure in very small quantity. The ortho-isomer predominates in the mixture of products, due to isomerization of cyclopentyl phenyl ether both in presence of phosphoric acid and aluminum chloride.

On the basis of our experiments the following reaction scheme is advanced:

$$C_6H_5OH + C_5H_9OH \xrightarrow[H_3PO_4]{AlCl_3} C_6H_5OC_5H_9 + o\text{-}C_5H_9C_6H_4OH + p\text{-}C_5H_9C_6H_4OH$$

$$\searrow$$

$$o\text{-}C_5H_9C_6H_4OH$$

EXPERIMENTAL

The substances used were freshly distilled phenol (b.p. 180°), phosphoric acid (d 1.86), commercial aluminum chloride, and cyclopentanol from adipic acid[13] with b.p. 137-138° (730 mm), d_4^{20} 0.9479, n_D^{20} 1.4530. Phenol was reacted with cyclopentanol in a three-necked flask fitted with thermometer, dropping funnel, mechanical stirrer and reflux condenser. Different orders of addition of reactants and of decomposition of reaction products were adopted depending on the catalyst used. Below are described three experiments carried out under the most different conditions.

Experiment 1. Phosphoric acid (16 ml) was added to fused phenol (9.4 g). A white solid mass, which did not become fluid until a temperature of 60° was reached. Cyclopentanol (8.6 g) was added in the course of 3 hr at 70°. The mixture was then heated for 5 hr at the same temperature and left overnight. It was then diluted with water and extracted with benzene to give a solution which was washed with water and treated with 20% NaOH solution. The insoluble phenate of the para-isomer came down. Decomposition of the phenate with hydrochloric acid gave 5.7 g (36%) of p-cyclopentylphenol with b.p. 115° (2 mm), m.p. 66-67°. According to [8] it has b.p. 155° (2 mm), m.p. 63-65°. From the alkali solution, after the decomposition with hydrochloric acid, was isolated 5.8 g (36.6%) of o-cyclopentylphenol with b.p. 110-111° (2 mm), m.p. 36°. Literature [11]: b.p. 137-140° (11 mm), m.p. 34-35°.

Redistillation of the nonphenolic portion gave 1.9 g (12%) of a fraction with b.p. 103-104° (1 mm) corresponding to o-cyclopentylphenol in properties. Redistillation of the nonphenolic fraction from all of the condensations with phosphoric acid (10 g) gave the following fractions: First, 85-90° (1 mm), 1.4 g (14%), a readily mobile liquid with a pleasant odor, insoluble in alkali; identical with cyclopentyl phenyl ether.

d_4^{20} 1.0186, n_D^{20} 1.5285, MR_D 49.06; calc. 48.85.
Found %: C 81.66; H 8.75. $C_{11}H_{14}O$. Calculated %: C 81.48; H 8.64.

Second fraction: 95-100° (1 mm), 2.8 g (28%), a colorless liquid with a rather pleasant odor, partly soluble in alkali.

d_4^{20} 1.0462, n_D^{20} 1.5450, MR_D 48.95; calc. 48.85.

This fraction is a mixture of cyclopentyl phenyl ether and o-cyclopentylphenol.

Third fraction: 106-107° (1 mm), 4.8 g (48%), a colorless liquid with a phenolic odor, soluble in alkali. Crystallizes as soon as crystals of o-cyclopentylphenol are added.

M.p. 36°, d_4^{20} 1.0615, n_D^{20} 1.5530, MR_D 48.96; calc. 48.73.

Experiment 2. In the course of 1.5 hr 13.4 g of aluminum chloride was added in small portions to 47 g of fused phenol at 70°. Hydrogen chloride came off violently. After HCl had ceased to be evolved, 8.6 g of cyclopentanol was added in the course of 3 hr at 70°, and heating of the mixture at the same temperature was continued for another 3 hr. The usual working-up with 20% alkali followed by distillation gave 7.1 g (46%) of the o- and p-cyclopentylphenol; b.p. 138-144° (15 mm).

The nonphenolic fraction with b.p. 120-140° (14 mm) weighed 1.4 g. Redistillation of this fraction gave 0.4 g (2.4%) of o-cyclopentylphenol with b.p. 107-110° (2 mm) and 0.5 g polycyclopentylphenols with b.p. 116-140° (2 mm).

Experiment 3. Aluminum chloride was added in small portions in the course of 1.5 hr at 30° to a mixture of phenol and cyclopentanol. After completion of the $AlCl_3$ addition, the mixture was heated for 3 hr at 50° and then stood overnight. The usual working-up gave 2.3 g (14%) of p-cyclopentylphenol with m.p. 64-65°, and 9.4 g (57.6%) of o-cyclopentylphenol with b.p. 119-120° (4 mm), m.p. 36°, d_4^{20} 1.0591, n_D^{20} 1.5550, MR_D 49.09; calc.

48.73. Nonphenolic fraction: 1.7 g with b.p. 110-160° (15 mm). Redistillation of the latter gave 0.5 g (3%) of o-cyclopentylphenol with b.p. 111-113° (2 mm) and 1 g of a substance with b.p. 158-163° (2 mm). The latter was not further investigated.

The following derivatives were prepared from p-cyclopentylphenol (m.p. 66-67°) and o-cyclopentylphenol (m.p. 36°):

1) Methyl ether of p-cyclopentylphenol [8], b.p. 98-99° (2 mm), d_4^{20} 1.0069, n_D^{20} 1.5331, MR_D 54.25; calc. 53.47.

Oxidation with 5% nitric acid gives anisic acid with m.p. 180° (from alcohol).

2) Methyl ether of o-cyclopentylphenol, b.p. 90-91° (3 mm), d_4^{20} 1.0144, n_D^{20} 1.5363, MR_D 54.12; calc. 53.47. Found %: C 82.10; H 9.6. $C_{12}H_{16}O$. Calculated %: C 81.81; H 9.09.

Ethyl ether of p-cyclopentylphenol, b.p. 110° (2 mm), d_4^{20} 0.9903, n_D^{20} 1.5253, MR_D 58.61; calc. 58.08. Found %: C 81.90; H 9.36. $C_{13}H_{18}O$. Calculated %: C 82.10; H 9.47.

2,4-Dinitro-6-cyclopentylphenol. Prepared by treatment of 1.62 g of o-cyclopentylphenol with 1.1 g of conc. H_2SO_4 at 60-70° [14], addition to the mixture of 3 ml of water, heating to 70°, and addition at this temperature of about 1 ml of HNO_3 (d 1.4). The mixture was diluted with another 2 ml of water and heated on a boiling-water bath for 1.5 hr. The next day yellow crystals came down (1.02 g) with m.p. 61.5-62° (from alcohol).

Found %: N 11.14. $C_{11}H_{12}O_5N_2$. Calculated %: N 11.11.

2,6-Dinitro-4-cyclopentylphenol. Prepared similarly: m.p. 76.5-77° (from alcohol).

Found %: N 11.40. $C_{11}H_{12}O_5N_2$. Calculated %: N 11.11.

p-Cyclopentylphenoxyacetic acid. Prepared in the usual manner [15], m.p. 116° (from ligroine). Literature [9]: m.p. 116°.

o-Cyclopentylphenoxyacetic acid. M. p. 112° (from ligroine). A mixed sample of the o- and p-acids gave a depressed melting point.

Found %: C 70.9; H 7.1. $C_{13}H_{16}O$. Calculated %: C 70.0; H 7.2.

p-Cyclopentylphenyl benzoate. Prepared by the published method [15], m.p. 93° (from alcohol).

Found %: C 81.3; H 6.6. $C_{18}H_{18}O$. Calculated %: C 81.2; H 6.7.

o-Cyclopentylphenyl p-nitrobenzoate. Prepared from o-cyclopentylphenol and p-nitrobenzoyl chloride [16], m.p. 77-78° (from alcohol).

Found %: N 4.55. $C_{18}H_{17}O_4N$. Calculated %: N 4.50.

SUMMARY

1. The possibility of alkylation of phenol with cyclopentanol in presence of aluminum chloride and phosphoric acid was demonstrated.

2. The main products of reaction in presence of $AlCl_3$ and H_3PO_4 are o- and p-cyclopentylphenols, the former predominating.

3. Cyclopentyl phenyl ether is also formed, but isomerizes to o-cyclopentylphenol in course of distillation.

4. The following new derivatives were prepared: methyl ether of o-cyclopentylphenol, ethyl ether of p-cyclopentylphenol, dinitro-o- and -p-cyclopentylphenols, o-cyclopentylphenoxyacetic acid, p-cyclopentylphenyl benzoate, and o-cyclopentylphenyl p-nitrobenzoate.

LITERATURE CITED

[1] A. R. Abdurasuleva, Zhur. Obshchei Khim. 28, 2992 (1958).*

[2] A. R. Abdurasuleva, Doklady Akad. Nauk Uzb. SSR 7, 39 (1957).

*Original Russian pagination. See C. B. translation.

[3] J. Braun and H. Deutsch, Ber. 45, 1267 (1912).

[4] N. Zelinskii and I. Tiz, Ber. 64, 183 (1931).

[5] S. S. Nametkin and E. S. Pokrovskaya, Zhur. Obshchei Khim. 8, 699 (1938).

[6] P. Cagniant, A. Deluzarche, and C. Chatelus, Zentr I, 729 (1947).

[7] C. A. Lutz, A. E. Bearse, J. E. Leonard, and F. C. Croxton, J. Am. Chem. Soc. 70, 4137 (1948).

[8] J. Braun, Liebigs Ann. 472, 62 (1929).

[9] E. McCreal, V. Niederl, and J. Niederl, J. Am. Chem. Soc. 61, 345 (1939).

[10] C. Mentzer, D. Mulho, and D. Xuong, Bull. Soc. Chim. 263 (1948).

[11] German Patent 615,448; Zentr. I, 884 (1936).

[12] A. R. Badler, J. Am. Chem. Soc. 75, 5967 (1953).

[13] Synth. Org. Preparations [in Russian] I, 518 (1949).

[14] Zentr I, 488 (1933).

[15] W. S. Johnson, R. D. Shannon, and R. A. Reed, Organic Reagents for Organic Analysis [Russian translation] (1948).

[16] Ref. Zhur. Khim. 39520 (1956).

CYCLOALKYLATION OF PHENOLS AND THEIR ETHERS

III. CONDENSATION OF p-CHLOROPHENOL WITH CYCLOHEXANOL

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4025-4027,

December, 1959

Original article submitted December 7, 1958

Direct alkylation of halophenols by cyclic alcohols has scarcely been studied. Only in a patent [1] is there mention of the possibility of preparation of cyclohexyl- and cyclopentylchlorophenols by condensation of the respective alcohols with chlorophenol in presence of $ZnCl_2$. Alkylation of p-chloro- and p-bromophenols by isobutene and tertiary-butyl chloride in presence of hydrochloric and sulfuric acids has been described [2, 3]. Reaction products were mono- and dialkylhalophenols. Condensation of o-chlorophenol with cyclohexene [4] in presence of BF_3 gave the isomeric cyclohexylchlorophenols. This reaction was studied in presence of $BF_3 \cdot (C_2H_5)_2O$ [5] and also in presence of $BF_3 \cdot H_3PO_4$ and $BF_3 \cdot (C_2H_5)_2O$ [6]. The sole products, irrespective of the reaction conditions and catalyst, were cyclohexyl halophenyl ethers. On the other hand, the alkylation of o-bromo-, p-bromo-, and chlorophenols with 2-butene [6] and 2-pentene [7] in presence of the same catalysts gave alkylhalophenols or mixtures of phenolic and ethereal products.

We studied the condensation of p-chlorophenol with cyclohexanol in presence of sulfuric acid of various concentrations (85, 93, and 98%) and of aluminum chloride. In presence of 85% H_2SO_4 (even in excess) no reaction takes place. Experiments under the conditions described for alkylation with olefins in presence of 98% acid did not give good results. Reactions in presence of 93% sulfuric acid were conducted withoug a solvent in excess of p-chlorophenol. Properties of components were one mole alcohol, 3 moles chlorophenol, and 2 moles acid. We varied the reaction duration and temperature while keeping the quantities of reactants constant. By reaction for 4-5 hr at 30-40° we were able to obtain yields of up to 56% of cyclohexylchlorophenol. Increasing reaction duration or raising of the temperature to 50-60° lowers the yield of cyclohexylchlorophenol and promotes formation of higher-boiling fractions consisting of dicyclohexylchlorophenols (~ 20%).

The influence of temperature, quantity and order of addition of reactants was studied during condensation in presence of aluminum chloride. The best results were obtained by addition of one mole $AlCl_3$ in small portions to 5 moles p-chlorophenol at 130-140°. After HCl had ceased coming off, one mole of cyclohexanol was added at the same temperature. The reaction mixture was next heated for 3,5-4 hr at 160-170°. Under these conditions the main reaction product was cyclohexylchlorophenol (65%); 2,6-dicyclohexylchlorophenol was also formed (~ 14%). Cyclohexyl chlorophenyl ether was not detected. Under our reaction conditions it evidently isomerizes completely to cyclohexylchlorophenol.

EXPERIMENTAL

Condensation of p-chlorophenol with cyclohexanol in presence of 93% sulfuric acid. Reactions were performed in a three-necked round-bottomed flask fitted with dropping funnel, thermometer, and mechanical stirrer. Cyclohexanol was added to the mixture of p-chlorophenol and sulfuric acid at the appropriate temperature. The mixture was stood until the next day at room temperature, then diluted with water and extracted with ether or

benzene; the extract was washed, and dried with calcium chloride. After the solvent and excess p-chlorophenol had been distilled off, the residue was fractionated. The following fractions were collected: First, b.p. 104-105° (12-13 mm)—p-chlorophenol; second, b.p. 170-175° (13 mm)—cyclohexylchlorophenol; third, b.p. 180-220° (13 mm)—dicyclohexylchlorophenol.

The yield from 38.5 g of p-chlorophenol, 10 g of cyclohexanol, and 20 g of sulfuric acid was 11.7 g of cyclohexylchlorophenol (~ 56%). In addition, 24 g of p-chlorophenol was recovered.

Condensation of p-chlorophenol with cyclohexanol in presence of aluminum chloride. To 64 g of p-chlorophenol at 130-140° was added 13.4 g of finely pulverized aluminum chloride in the course of 2 hr. The mixture became very viscous. Much HCl came off at the start of addition of $AlCl_3$. The reaction mass was heated for another 1.5 hr, and then 10 g of cyclohexanol was added from a dropping funnel in the course of 2 hr at 150-160°. Then the mixture was heated for another 4 hr at the same temperature. The next day the mixture was worked up in the usual manner. The benzene solution of the reaction products was treated with 20% alkali [8]. From the insoluble phenate was isolated 13.7 g (65%) of 2-cyclohexyl-4-chlorophenol with b.p. 146-148° (5-6 mm) and m.p. 55° (from ligroine). The alkali solution contained the excess of p-chlorophenol. From the benzene solution was isolated only 2 g (14%) of 2,6-dicyclohexyl-4-chlorophenol with b.p. 180-200° (6 mm).

Identification of reaction products. The fractions of 2-cyclohexyl-4-chlorophenol from all of the condensations (in presence of $AlCl_3$) were combined and redistilled in vacuo. B.p. 146-148° (6 mm), m.p. 55° (from ligroine); small, lustrous needles. Redistillation of cyclohexylchlorophenol fractions obtained in presence of H_2SO_4 gave a product with b.p. 140-142° (2 mm), m.p. 56° (from ligroine). A mixture of the two products did not have a depressed melting point.

2-Cyclohexyl-4-chlorophenoxyacetic acid [9] was prepared by the usual method [9]; m.p. 167-168° (from ligroine).

2-Cyclohexyl-4-chlorophenyl p-nitrobenzoate was prepared in similar fashion to the dinitrobenzoate [10]. At 20°, one g of p-nitrobenzoyl chloride was added to the phenate, prepared from one g of cyclohexylchlorophenol and 0.1 g of metallic sodium in 2 ml of absolute ether. The reaction was very violent and the mixture had to be cooled. The nitrobenzoate, isolated by the usual procedure, had m.p. 115° (from alcohol).

Found %: N 3.73. $C_{19}H_{18}O_4NCl$. Calculated %: N 3.89.

Methyl ether of 2-cyclohexyl-4-chlorophenol was prepared in the usual manner.

B.p. 136-137° (6 mm), d_4^{20} 1.122, n_D^{20} 1.5447, MR_D 63.14; calc. 62.94.
Found %: C 69.17; H 7.70; Cl 16.33. $C_{13}H_{17}OCl$. Calculated %: C 69.48; H 7.57; Cl 15.81.

2,6-Dicyclolexyl-4-chlorophenol. A mixture from all of the condensations, b.p. 118-120° (6 mm) and 118-220° (13 mm), crystallized after standing for a long period. M. p. 100-101° after two recrystallizations from aqueous alcohol.

Found %: C 73.76; H 8.81; Cl 12.26. Active H number 1.14, 1.08 [11]. $C_{18}H_{25}OCl$. Calculated %: C 73.84; H 8.56; Cl 12.13. Active H number 1.

SUMMARY

1. The possibility was demonstrated of alkylation of p-chlorophenol with cyclohexanol in presence of 93% sulfuric acid and aluminum chloride.

2. The main reaction products are 2-cyclohexyl-4-chlorophenol (56-65%), and 2,6-dicyclohexyl-4-chlorophenol (14-20%); the latter is not described in the literature.

3. Cyclohexylchlorophenyl p-nitrobenzoate and the methyl ether of cyclohexylchlorophenol are described for the first time.

LITERATURE CITED

[1] German Patent 615448; Chem. Zentr. I, 884 (1936).

[2] H. Hart, J. Am. Chem. Soc. 71, 1966 (1949).

[3] H. Hart and F. Cassis, J. Am. Chem. Soc. 73, 3179 (1951).

[4] P. Lewas, Ann. chim. 3, 145 (1943).

[5] S. V. Zavgorodnyi, Zhur. Obshchei Khim. 22, 1995 (1952).•

[6] S. V. Zavgorodnyi and V. G. Kryuchkova, Zhur. Obshchei Khim. 27, 330 (1957).•

[7] S. V. Zavgorodnyi and E. M. Faustova, Zhur. Obshchei Khim. 23, 1651 (1953).•

[8] A. R. Abdurasuleva, Zhur. Obshchei Khim. 28, 2992 (1958).•

[9] S. S. Nametkin, N. N. Mel'nikov, Yu. A. Baskakova, and K. S. Bakarov, Zhur. Anal. Khim. 5, 7 (1950).

[10] Ref. Zhur. Khim. 39520 (1956).

[11] A. P. Terent'ev, N. G. Avakyan, and E. A. Terent'eva, Vestnik Moskov. Gosudar. Univ. 6 (1949).

•Original Russian pagination. See C. B. translation.

FUNCTIONAL DERIVATIVES OF MALONALDEHYDE AND THEIR REACTIONS*

X. ACETALS OF HOMOLOGS OF MALONALDEHYDE

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4027-4029, December, 1959

Original article submitted December 11, 1958

Full acetals of malonaldehyde, formed by condensation of vinyl ethers with orthoformic esters [2], are convenient starting substances for many syntheses, including those of the simplest heterocyclic compounds of the pyrazole, isoxazole, and pyrimidine series [3]. It was of interest to synthesize acetals of homologs of malonaldehyde, since these could further enlarge the synthetic possibilities and also provide a new and convenient route to substituted malonaldehydes. The only members of the latter group so far investigated in detail are methylmalonaldehyde [4] and phenylmalonaldehyde [5].

One general method of preparation of homologs of malonaldehyde has been known up to now [6]; this is based on alkali decomposition of α-alkyl-β-dimethylaminoacroleins, which are obtained by reaction of vinyl ethers or the corresponding acetals with the product of interaction of dimethylformamide and phosgene.

We showed that full acetals of homologs of malonaldehyde can be obtained in satisfactory yields by the action of orthoformic ester on alkylalkenyl ethers in presence of catalytic quantities of Friedel-Crafts catalysts (zinc chloride, aluminum fluoride etherate, boron trifluoride etherate, etc.). The reaction proceeds according to the general equation:

$$RCH{=}CHOR' + HC(OR')_3 \xrightarrow{(C_2H_5)_2O \cdot BF_3} \underset{(I)}{RCH[CH(OR')_2]_2}$$

R = alkyl or aryl, R' = alkyl

A two- to fourfold excess of orthoformic ester is desirable in order to suppress the parallel reaction of acetal (I) with alkylalkenyl ether with formation of compounds with the general formula $(R'O)_2CH[CHR\ CH(OR')]_nOR'$. At the conclusion of the reaction (slightly exothermic), the catalyst is neutralized by addition of anhydrous sodium carbonate, and acetals (I) are isolated by fractionation. They are stable liquids that distill without breakdown and can be kept for a long period. Under the action of aqueous acid solutions, acetals (I) readily release the free dialdehydes; the latter can either be used directly for required transformations or (if necessary) can be isolated in the pure state via the sodium or copper salt.

EXPERIMENTAL

Starting substances. The alkenyl ethers were prepared by heating the corresponding acetals in presence of sodium bisulfate, aniline sulfate, or sulfanilic acid [7].

* For preceding communication see [1].

1,1,3,3-Tetraethoxy-2-methylpropane. To a solution of 0.14 ml of boron trifluoride etherate in 29.6 g of ethyl orthoformate was added 8.6 g of propenylethyl ether [7], with stirring, in 10-15 min at 30-35°; during this operation the temperature of the mixture rose to 45° and the mixture was stirred at this temperature for an hour. It was cooled to room temperature, 1 g of anhydrous sodium carbonate was added, and stirring was continued for 3 hr. The precipitate was filtered and the filtrate fractionated in vacuo. Ethyl orthoformate was recovered in the amount of 21 g [b.p. 63° (40 mm)] and 12.6 g (53.4%) of 1,1,3,3-tetraethoxy-2-methylpropane was obtained.

B.p. 87-87.5° (5 mm), d_4^{20} 0.9158, n_D^{20} 1.4151, MR_D 64.06; calc. 64.18.
Found %: C 61.34, 61.34; H 11.24, 11.21. $C_{12}H_{26}O_4$. Calculated %: C 61.53; H 11.18.

Methylmalonaldehyde. A mixture of 1 g of 1,1,3,3-tetraethoxy-2-methylpropane, 1 ml of 1 N hydrochloric acid solution, and 2 ml of water was heated for 45 min (bath temperature 60-70°); sodium hydroxide solution was added until the mass had a pH of 8, and the liquid was evaporated to dryness in vacuo. The dry residue was dissolved in 10 ml of anhydrous alcohol, and the solution was filtered; the sodium salt of methylmalonaldehyde was precipitated by addition of benzene; the salt (0.4 g) was suspended in 10 ml of absolute ether, and 2 ml of ether saturated with hydrogen chloride was added. After shaking for 10 min, the precipitate was filtered off and the filtrate evaporated. There was obtained 0.18 g of methylmalonaldehyde with m.p. 83-85°, rising to 88-89° after sublimation in vacuo.* Literature [4]: m.p. 89°.

Methylmalonaldehyde dianil. A mixture of 1.17 g of 1,1,3,3-tetraethoxy-2-methylpropane, 0.93 g of aniline, 1.5 ml of concentrated hydrochloric acid, 2 ml of water, and 1.5 ml of alcohol was refluxed for 30 min. Light-yellow crystals of the dianil hydrochloride came down on cooling and were filtered and washed with cooled alcohol. Yield 1 g (73.3%), m.p. 223-224°.

Found %: N 10.57, 10.58; Cl 12.86, 12.72. $C_{16}H_{16}N_2 \cdot HCl$. Calculated %: N 10.30; Cl 13.01.

The methylmalonaldehyde dianil hydrochloride was converted to the base by treatment with 10% aqueous solution of sodium carbonate; yield 0.8 g of base with m.p. 240-250° (decomp.).

Found %: N 11.66, 11.60. $C_{16}H_{16}N_2$. Calculated %: N 11.85.

1,1,3,3-Tetramethoxy-2-methylpropane. Prepared in similar fashion to the tetraethoxy derivative from 24 g of methyl orthoformate, 0.14 g of boron trifluoride etherate, and 7.2 g of propenylmethyl ether. Yield 7.1 g (39.8%).

B.p. 62-63° (5 mm), n_D^{20} 1.4090, d_4^{20} 0.9652, MR_D 45.65; calc. 45.71.
Found %: C 54.53; H 10.51. $C_8H_{18}O_4$. Calculated %: C 53.92; H 10.18.

The following substances were similarly prepared:

1,1,3,3-Tetraethoxy-2-ethylpropane (yield 64%).

B. p. 82-83° (3 mm), d_4^{20} 0.9097, n_D^{20} 1.4179, MR_D 68.78; calc. 68.80.
Found %: C 62.99, 63.07; H 11.70, 11.57. $C_{13}H_{28}O_4$. Calculated %: C 62.87; H 11.37.

Ethylmalonaldehyde (yield 50%), m.p. 72-73°. Literature [6]: m.p. 69-70° (corr.).

Methylmalonaldehyde dianil hydrochloride (yield 71.4%), m.p. 212-213°. Literature [6]: m.p. 206-207° (corr.).

Found %: Cl 12.65, 12.81. $C_{17}H_{18}N_2 \cdot HCl$. Calculated %: Cl 12.37.

1,1,3,3-Tetraethoxy-2-isopropylpropane (yield 68.0%).

B.p. 80-81.5° (2 mm), d_4^{20} 0.9107, n_D^{20} 1.4220, MR_D 73.21; calc. 73.42.
Found %: C 64.55, 64.66; H 11.66, 11.76. $C_{14}H_{30}O_4$. Calculated %: C 64.10; H 11.53.

Isopropylmalonaldehyde dianil hydrochloride (yield 73.3%), m.p. 167-171°.

Found %: Cl 12.07, 11.97; N 9.14, 9.32. $C_{18}H_{20}N_2 \cdot HCl$. Calculated %: Cl 11.79; N 9.30.

* All melting points are uncorrected.

Isopropylmalonaldehyde. A mixture of 1 g of 1,1,3,3-tetraethoxy-2-isopropylpropane, 1 ml of 1 N hydrochloric acid and 2 ml of water was heated for 45 min at 45°; after cooling, copper acetate solution was added, and the mass extracted with chloroform. The chloroform was evaporated and the residue suspended in ether and shaken with 2 ml of 5 N sulfuric acid. Removal of the ether left 0.2 g (46.5%) of isopropylmalonaldehyde with m.p. 62-63°. Literature data [6]: m.p. 62-63° (corr.).

1,1,3,3-Tetraethoxy-2-phenylpropane (yields 43.9%).

B.p. 125-127° (1.5-2 mm), d_4^{20} 0.9826, n_D^{20} 1.4715, MR_D 84.36; calc. 83.66.
Found %: C 69.54, 69.56; H 9.39, 9.32. $C_{17}H_{28}O_4$. Calculated %: C 68.90; H 9.49.

Phenylmalonaldehyde dianil hydrochloride (yield 71.8%), m.p. 143-144°.

Found %: N 8.22, 8.42. $C_{21}H_{18}N_2 \cdot HCl$. Calculated %: N 8.36.

Phenylmalonaldehyde (yield 28%, prepared in similar fashion to isopropylmalonaldehyde), m.p. 93.5-94.5° (from water). The copper salt of phenylmalonaldehyde melts at 214-215°. Literature [5]: m.p. 95°.

SUMMARY

Reaction of alkenyl ethers with orthoformic ester in presence of boron trifluoride etherate gave acetals of homologs of malonaldehyde $(AlkO)_2CHCHRCH(OAlk)_2$, where R = CH_3, C_2H_5, iso-C_3H_7, or C_6H_5.

LITERATURE CITED

[1] T. V. Protopopova and A. P. Skoldinov, Zhur. Obshchei Khim. 29, 3982 (1959).*

[2] U. S. Patent 2500486; C. A. 1950, 5379; U. S. Patent 2502433; C. A. 1950, 6430; U. S. Patent 2517543; C. A. 1951, 1166; U. S. Patent 2527533; C. A. 1951, 1622; U. S. Patent 2556312; C. A. 1952, 1031; U. S. Patent 2549076; C. A. 1949, 4291; T. V. Protopopova and A. P. Skoldinov, Zhur. Obshchei Khim. 27, 57 (1957).*

[3] T. V. Protopopova and A. P. Skoldinov, Zhur. Obshchei Khim. 27, 1276 (1957).

[4] P. Pino, Gazz. 80, 768 (1950); 81, 757 (1951).

[5] H. Rupe and E. Knap, Helv. Chim. Acta 10, 299, 847 (1927).

[6] Z. Arnold and F. Šorm, Coll. of Czech. Chem. Comm. 23, 452 (1958).

[7] M. G. Voronkov, Zhur. Obshchei Khim. 20, 2060 (1950).*

*Original Russian pagination. See C. B. translation.

CONDENSATIONS IN PRESENCE OF BORON TRIOXIDE

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4030-4035,

December, 1959

Original article submitted December 22, 1958

One of us [1] found that "boron acetate" is a catalyst for condensations of aromatic aldehydes with acetic anhydride.

In the present work we condensed benzaldehyde with various carboxylic acid anhydrides, using boron trioxide as catalyst. The latter evidently reacts with the carboxylic acid anhydride to form an acyl borate analogous to boron acetate. Boron trioxide rapidly goes into solution, and the synthesis of cinnamic acid proceeds identically in presence of boron trioxide and boron acetate. Among the products found after completion of the reaction and treatment of the mixture with methanol was trimethyl borate. This is evidently formed by reaction of methanol with the boron acetate present [2].

The over-all reaction equation is:

$$C_6H_5CHO + 2(RCH_2CO)_2O \longrightarrow C_6H_5CH{=}\underset{\displaystyle R}{\overset{\displaystyle |}{C}}{-}COOCH_2R + 2RCH_2COOH.$$

The study of the synthesis of cinnamic acid established the necessity for a catalytic quantity of boron trioxide not stoichiometrically bound up with the reaction equation. The acetic acid formed in the cinnamic acid synthesis should preferably be distilled off; an excess of acetic anhydride is not needed and is even harmful, since it lowers the yield. Homologs of cinnamic acid are obtained under milder conditions; the acid formed cannot be distilled, since the reaction products resinify at the necessary temperatures. For this reason the synthesis must be carried out with a slight excess of carboxylic acid anhydride. The reaction can also be carried out with anhydrides of dibasic acids—succinic and adipic.

With increasing molecular weight of the acid anhydride, the yield of the corresponding alkylcinnamic acid decreases, but it is usually higher than in the classic Perkin reaction: α-isopropylcinnamic acid was obtained in a yield of 31.6 instead of 13% by the classic variant [3]. The crotonic condensation can also be realized in presence of boron trioxide when carried out at above 120° (usually it proceeds at 140-150°). The reaction is performed in a Dean—Stark apparatus, using xylene as auxiliary liquid for entrainment of water. The reaction mass always contains high-boiling substances (evidently products of interaction with boron trioxide). The boiling ranges of the distilled fractions were very wide, but on redistillation the various products came over at the temperatures reported in the literature. This method led to good yields of chalcone, dypnone and α-cyclohexylidenecyclohexanone. Benzylidenemalonic ester is similarly prepared. The method is simple and convenient for preparative purposes.

The course of the crotonic condensation is evaluated from the quantity of water distilled off (see figure). The reaction is homogeneous, and the mass is stirred at the boil. On the basis of the velocity constant calculated from the amount of water distilled during formation of dypnone, on the assumption of a first-order reaction, we find that K is about 0.24 in the middle of the curve. In other cases K is not constant under the reaction conditions.

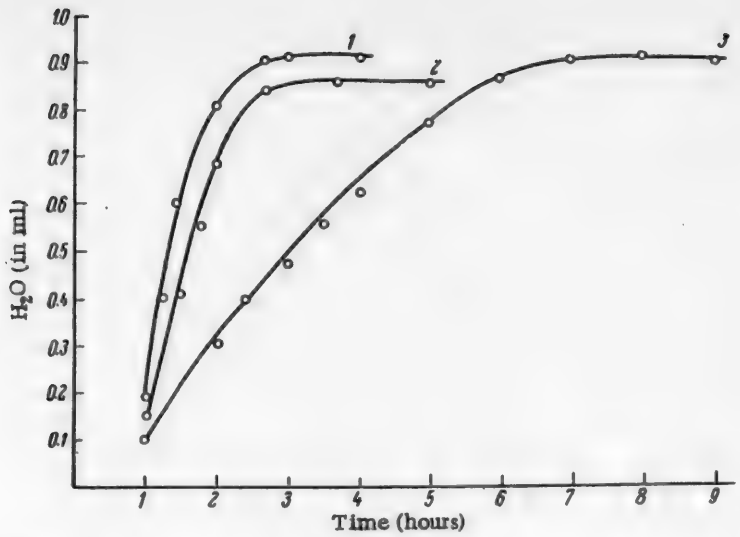
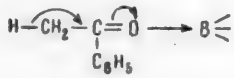


Figure Quantity of water distilled during the crotonic condensation. Syntheses: 1) α-Cyclohexylidenecyclohexanone; 2) benzylideneacetophenone (chalcone); 3) α-methylbenzylideneacetophenone (α-methylchalcone).

Boron acetate (and other acyl borates) and boron trioxide evidently catalyze the above reactions like other "aprotonic" acids—in particular boron trifluoride [4]. In the crotonic condensation or the condensation of aldehydes with anhydrides, the carbonyl group of the aldehyde is activated by the following mechanism.

The resulting electrophilic complex can add on a molecule with labile hydrogen atoms. The added molecule can in turn be activated by the boron compound according to the α−π conjugation mechanism.



The first reaction step gives, as in the other cases, a hydroxy compound (an aldol) which then splits off water.

We assume that the labile hydrogen is activated. In that event, the mechanism of the crotonic condensation catalyzed by "aprotonic" acids becomes similar to that of the condensation catalyzed by bases; this is extremely probable. We see (from the figure) that the reaction of formation of benzylideneacetophenone is faster than that of formation of dypnone, and no traces of dypnone are present with the former substance; interaction with the boron compound evidently results in acetophenone reacting as a molecule with a labile hydrogen, i.e., as the second component.

The aldehyde molecule is similarly activated in the condensation of aldehydes with acid anhydrides. At the same time the mobility of the hydrogen at the α-carbon atom is again increased due to interaction with the boron atom. For the case of acetic anhydride this can be represented by:

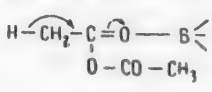


TABLE 1

Condensation of Benzaldehyde* with Carboxylic Acid Anhydrides in Presence of Boron Trioxide (Boron Acetate and Its Homologs)

Prep. no.	Anhydride		Boron trioxide (in g)	Reaction conditions		Reaction product: acid	Yield (%)	Melting point	Source
	name	quantity		temperature in mass	time				
1	Acetic	18	0.45	to 160–170°	3–3.5	Cinnamic	80	131–132°	[5]
2		18	0.45		3–3.8		78	131–132	
3		18	0.90		3–3.5		62	131–132	
4		18	0.22		3–3.5		40	131–132	
5		13	0.45		3.5		60	131–132	
6		22	0.45		3.5		78	131–132	
7	Propionic	23.5	0.45	165	8	α-Methylcinnamic	56.2	74	[8]
8	Butyric	31.6	1.4		8	α-Ethylcinnamic	42	104	
9	Isovaleric	37.2	1.4		8	α-Isopropylcinnamic	31.6	117	[9]
10	Succinic	10.6	2	150	6	α-Benzylidenesuccinic	16	191 (after three recrystallizations from EtOH	[10]
11	Adipic	12.8	2		8	α-Benzylideneadipic	—	174 from EtOH	[11]

* In each experiment 10.6 g of benzaldehyde was taken.

In its subsequent course the reaction resembles the crotonic condensation. Condensation of aromatic aldehydes with acid anhydrides in presence of boron acetate is faster and more complete than in the Perkin reaction (in presence of a metallic acetate) even though boron acetate is present in catalytic amount. In the synthesis of cinnamic acid, hardly any unreacted benzaldehyde remains, but noncrystalline products are obtained in the form of light-yellow resin—probably products of further condensation; they decompose on distillation in vacuo to give a little cinnamic acid. It may be recalled that cinnamic acid is formed in negligible amount when the reaction is performed in presence of boron fluoride in the cold [3].

The present investigation and earlier work show that at higher temperatures (usually 140-200°) derivatives of boric acid are active catalysts (like strong acids) in condensation [1] and esterification [5] reactions.

In the latter case the polyboric acids exerting the catalytic action evidently also react like "aprotonic" acids. In the present work we found that esterification also takes place in presence of boron trioxide, in harmony with the hypothesis put forward.

It is probable that during esterification of carboxylic acids in presence of boron trioxide or polyboric acids, a molecule of carboxylic acid (a) is activated by the acid catalysis mechanism and a molecule of alcohol (b) by the mechanism established [6] for esterification in presence of acids.

(a) (b)

The susceptibility of boric acid to complex formation with alcohols is well known. Esterification proceeds at a relatively high temperature and in presence of a considerable quantity of boron trioxide (or acid). If we assume

TABLE 2

Condensation in the Presence of Boron Trioxide*

Expt. no.	Starting substances		Quantity of xylene (ml)	Reaction conditions		Quantity of water of reaction (ml)	Substance obtained		Characteristic	Literature	Remarks
	name	quantity (in g)		temperature	duration (hr)		name	yield (%)			
1	Benzaldehyde Acetophenone	5.3 6	30	140°	2	0.8	Benzylideneacetophenone (chalcone)	87	M.p. 57° (from alcohol), no depression in mixed melting test	[12]	200-220° (13 mm) fraction collected. 10.8 g of crude product obtained
2	Acetophenone	12	30	140	9	0.9	Methylbenzylideneacetophenone (dypnone)	87	B.p. 205-210° (15 mm), semicarbazone m.p. 151°	[13]	5.8 g of acetophenone recovered. Yield calculated on acetophenone reacted
3	Cyclohexanone	9.8	30	140	2	0.8	α-Cyclohexylidenecyclohexanone	76.4	B.p. 123-125° (5 mm), semicarbazone m.p. 175°	[14,15]	10 g of crude product obtained, b.p. 180-200°
4	Benzaldehyde Malonic ester	5.3 8	15	150	4.5	0.9	Benzylidenemalonic ester	77	B.p. 185-186° (17 mm), n_D^{20} 1.5347	[16]	

* In each experiment one g of boron trioxide was taken.

that the medium has a high acidity under these conditions, then another reaction mechanism is also possible involving formation of RCO^+ cations, as suggested for esterification in a strongly acid medium, and in particular for esterification in presence of excess of boron fluoride [7]. However, the latter mechanism is less probable.

EXPERIMENTAL

Condensation of Benzaldehyde with Acid Anhydrides

Synthesis of cinnamic acid and its homologs. Benzaldehyde (10.6 g), acetic anhydride (18 g), and boron trioxide (0.45 g) were placed in a flask fitted with a Vigreux column 10 cm high. After 3-3.5 hr the acetic acid was distilled off at a temperature not higher than 120-123°. After distillation was complete (11-12 g distilled) and the temperature of the mass had risen to 160-170°, the reaction was stopped. To the reaction mass (a viscous, dark-brown liquid) were added 9 ml of methanol and 2 ml of water, the cinnamic anhydride thereby being hydrolyzed and the boron acetate converted to trimethyl borate. A mixture of methanol and trimethyl borate was distilled off on a water bath. The residue was extracted several times with 50% methanol until crystals of cinnamic acid ceased to be deposited on cooling; yield 11.8 g (78%), m.p. 131-132°. The cinnamic acid could be isolated by vacuum distillation, immediately after distillation of the methanol and trimethyl borate, at 165-175° (10 mm); partial decomposition occurred towards the end. The product was washed with water and dried; m.p. 131-132° (in agreement with the literature); yield 12 g (80%).

Results of experiments on preparation of cinnamic acid and its analogs are presented in Table 1. The yield of cinnamic acid falls if the amount of boron trioxide is decreased or increased.

Homologs of cinnamic acid were synthesized in a similar manner (but without distillation of the acid formed) by simple refluxing. The hot mixture was washed in 200 ml of water and neutralized with sodium bicarbonate; unreacted benzaldehyde (about 1 g) was distilled off with steam. The residue was boiled with active carbon and filtered; the filtrate was poured into a mixture of hydrochloric acid and ice. The precipitated cinnamic acid was stood overnight, filtered, and dried.

Benzylidenesuccinic and α-benzylideneadipic acids were synthesized in a Dean–Stark apparatus with addition of 50 ml of xylene for entrainment of the water of reaction. When the theoretical quantity of water (1.8 ml) had been taken off, the reaction was stopped. Further treatment was the same as for the preparation of cinnamic acid homologs.

The prepared acids were tested for purity by titration with 0.1 N alkali in presence of phenolphthalein. In each case, values of $100 \pm 0.3\%$ were obtained.

Crotonic condensation in presence of boron trioxide. Preparations were carried out in a Dean–Stark apparatus. The mixture of reactants and xylene was boiled on a sand bath until the optimum quantity of water had been removed. The product was isolated by vacuum distillation of the reaction mass and purified by redistillation. Results are given in Table 2. The characteristics found were in agreement with those reported in the literature.

Esterification in presence of boron trioxide. Reactions were run in a flask fitted with thermometer and dropping funnel (Dean–Stark apparatus). Benzoic acid (31 g, 0.25 mole), isoamyl alcohol (60 g) with b.p. 130-132°, and boron trioxide (1.8 g) were heated to 180°, and 60 g of isoamyl alcohol was added dropwise at such a rate that the temperature was 180-200° but fell to 160° towards the close of the reaction. After 6-7 hr the release of water could be considered complete. The reaction mixture was then diluted with 100 ml of benzene, washed with water, with 3% sodium carbonate solution, and again with water; it was finally dried with anhydrous magnesium sulfate and distilled to give 38 g (75%) of isoamyl benzoate with b.p. 263-254°, in agreement with the literature [5].

SUMMARY

1. Benzaldehyde undergoes condensation to cinnamic acids in presence of boron acetate (or its analogs).

2. Crotonic condensation is successfully effected in presence of boron trioxide if the reaction temperature is 140° and higher.

3. Mechanisms of the reactions in question are proposed.

LITERATURE CITED

[1] V. K. Kuskov, Doklady Akad. Nauk SSSR 110, 223 (1956).*

[2] A. Pictet and A. Geleznow, Ber. 36, 2225 (1900).

[3] Orga. ic Reactions, I [in Russian] (1948).

[4] D. S. Breslow and C. R. Hauser, J. Am. Chem. Soc. 62, 2385 (1940).

[5] V. K. Kuskov and V. A. Zhukova, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk 737 (1956).*

[6] H. Meerwein and G. Hinz, Lieb. Ann. 484, 1 (1930); cf. W. Hückel, Theoretical Principles of Organic Chemistry [Russian translation] (IL, 1955), p. 545.

[7] H. S. Booth and D. R. Martin, Chemistry of Boron Fluoride and its Derivatives [Russian translation] (IL, 1955) p. 184; A. V. Topchiev, S. V. Zavgorodnii, and Ya. M. Paushkin, Boron Fluoride and Its Compounds as Catalysts in Organic Chemistry [in Russian] (Izd. AN SSSR, 1956).

[8] D. S. Breslow and C. R. Hauser, J. Am. Chem. Soc. 61, 786 (1939).

[9] A. Schaarschmidt, E. Georgeapol, and I. Herzenberg, Ber. 51, 1060 (1918).

[10] H. Stobbe and O. Horn, Ber. 41, 3983, 4354 (1908).

[11] R. Poggi and V. Guastalla, Gazz. 61, 405 (1931).

[12] N. O. Calloway and L. D. Green, J. Am. Chem. Soc. 59, 809 (1937).

[13] N. O. Calloway and L. D. Green, J. Am. Chem. Soc. 59, 610 (1937).

[14] O. Wallach, Ber. 29, 2965 (1896).

[15] J. Peesek, Coll. of Czech. Chem. Comm. 21, 375 (1956).

[16] H. Staudinger, Lieb. Ann. 341, 110 (1905).

*Original Russian pagination. See C. B. translation.

THE DIRECTIVE ACTION OF SUBSTITUENTS DURING OXIDATION OF QUATERNARY PHENAZINE SALTS. ARYLPHENAZINONES

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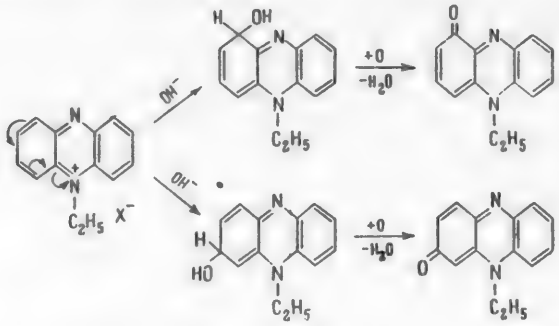
Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4036-4045, December, 1959

Original article submitted December 18, 1958

Quaternary phenazonium salts readily enter into nucleophilic substitution reactions. It has been shown that the presence of a cationic charge in a quaternary phenazonium salt at the nitrogen atom in position 10 causes build-up of electrons in positions 1 and 3 [1]. In an aqueous alkaline medium nucleophilic OH^- groups add on to give poorly stable 1,10- or 3,10-dihydro products which oxidize to N-alkylphenazinones; photochemical oxidation gives blue 10-alkylphenazinones-1, while oxidation with chemical agents gives red 10-alkylphenazinones-3.

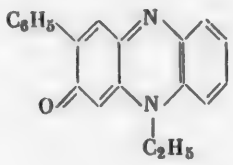


It is understandable that introduction of electron-donating or electron-accepting substituents will alter the distribution of the electron densities of the ring in positions 1 and 3, and that addition of nucleophilic agents in these positions can be facilitated, hindered, or completely suppressed. In some earlier studies quaternary salts of unsubstituted phenazine containing different alkyl radicals at the nitrogen atom were subjected to oxidation [2]; in such cases the radical had little influence on the distribution of electron densities in the ring. Oxidation studies have also been made on quaternary phenazonium salts containing alkoxy groups in the α and β positions [3]. The influence of electron-accepting substituents on the formation of phenazinones has scarcely been studied, and no work at all has been done on the influence of the C_6H_5 group.

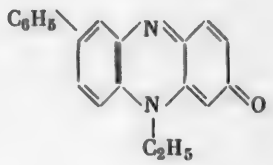
In the present work an attempt was made to establish the preferred direction of oxidation of quaternary salts of 1- and 2-phenylphenazines, to establish which ring is the more easily oxidized (the substituted or the unsubstituted one), and to observe the influence on the oxidation behavior of the presence of alkoxy groups.

We had at our disposal specimens of quaternary salts of 1- and 2-phenylphenazines and also salts of 1-phenyl-6-methoxy- and 2-phenyl-6-methoxyphenazines. By oxidation of these by the McIlwain method we obtained a series of red phenazinones whose structure was established by reverse synthesis. The preparations were characterized by the melting and decomposition points and by the absorption spectra.

Chromatographic examination of the product of oxidation of the quaternary salt of 2-phenyl-10-ethylphenazine (using potassium ferricyanide as oxidant in an alkaline medium) led to isolation of only one red phenazinone with m.p. 175°. This substance had absorption maxima at 242, 292, 377, and 530 mμ. Its structure is represented by either (I) or (II).

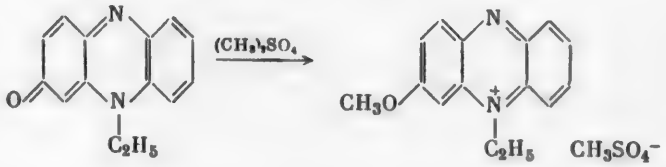


(I) 2-phenyl-10-ethylphenazinone-3



(II) 2-phenyl-10-ethylphenazinone-6

N-Alkylphenazinones are known to enter into reaction with dimethyl sulfate to form quaternary salts of methoxyphenazine [4].



We applied this reaction to the phenazinone of unknown structure that had been prepared, and we obtained 2-phenyl-(X)-methoxy-10-ethylphenazonium perchlorate (III) with m.p. 248°, decomp. p. 257°, and absorption maxima in alcoholic solution at 270, 286, and 448 mμ (Fig. 1). The structure of this salt was elucidated by comparison with a preparation of 2-phenyl-6-methoxy-10-ethylphenazonium perchlorate (IV) which had m.p. 223°, decomp. p. 233°, and absorption maxima in alcohol at 288, 398, and 485 mμ (Fig. 1).

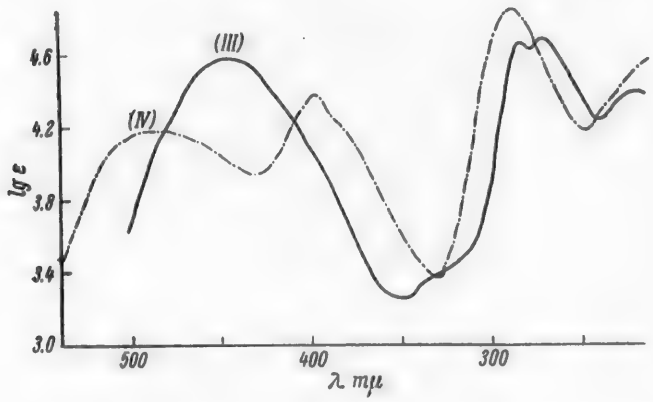
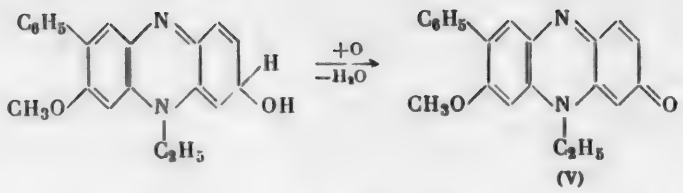


Fig. 1. Absorption spectra of (III) and (IV) in alcohol (1.5-3 × × 10^{-5} mole/liter).

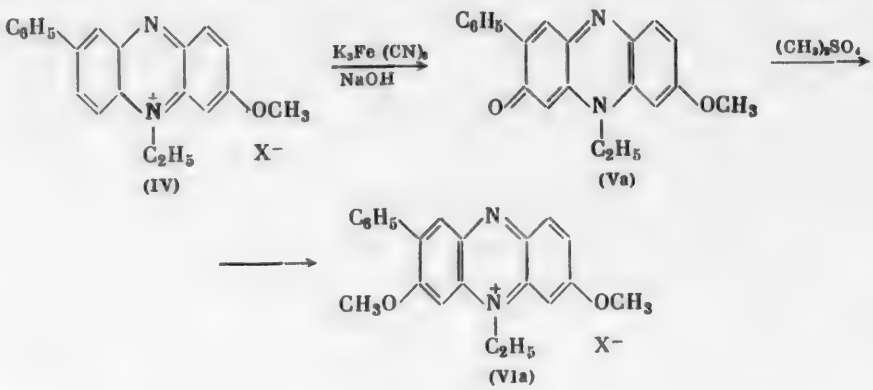
It follows from the difference in absorption spectra and melting and decomposition points of salts (III) and (IV) that salt (III) has the structure of 2-phenyl-3-methoxy-10-ethylphenazonium perchlorate, and that accordingly the phenazinone must be assigned the structure (I)—2-phenyl-10-ethylphenazinone-3.

In the course of further oxidation of (III) with potassium ferricyanide in alkali solution, the hydroxyl ion adds on in the 6 position; oxidation yields a single product—2-phenyl-3-methoxy-10-ethylphenazinone-6 (V).



(V)

This preparation was converted by the action of dimethyl sulfate into 2-phenyl-3,6-dimethoxy-10-ethylphenazonium perchlorate (VI), whose structure was confirmed by reverse synthesis according to the scheme:



(IV) (Va) (VIa)

Preparations (VI) and (VIa) have identical absorption spectra (Fig. 2), melting points and decomposition points; their mixture melts without depression.

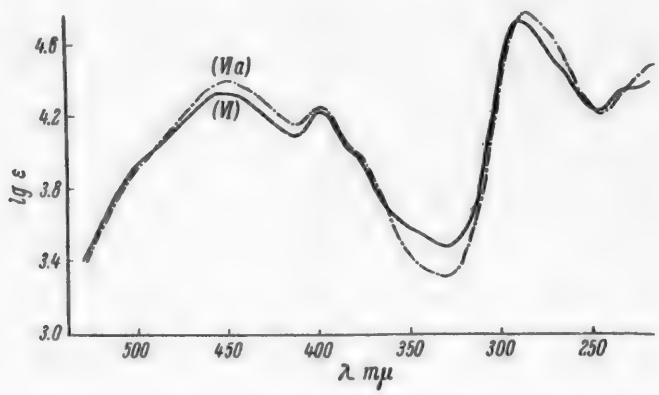
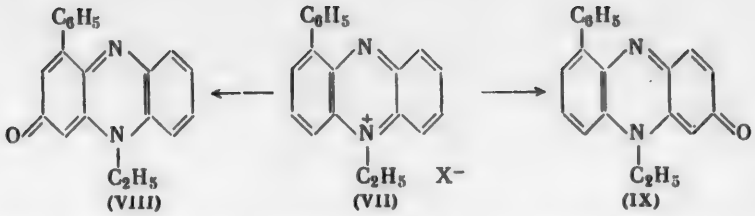


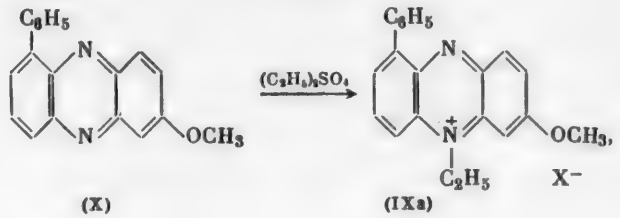
Fig. 2. Absorption spectra in alcohol of (VI) (2.5-5 x 10^{-5} mole/liter) and (VIa) (2.0-2.5 x 10^{-5} mole/liter).

Consequently, in the oxidation of a quaternary salt of 2-phenyl-10-ethylphenazine, the nucleophilic agent enters the benzene ring in which the phenyl grouping is located, intensifying the electron density and thereby facilitating oxidation of the quaternary salt molecule. Only on further oxidation does the second benzene ring react in position 6.

Oxidation of quaternary salts of 1-phenylphenazine. Oxidation of a quaternary salt of 1-phenyl-10-ethylphenazine (VII) can lead to two possible phenazinones: 1-phenyl-10-ethylphenazinone-3 (VIII) and 1-phenyl-10-ethylphenazinone-6 (IX):



In our experiments only one isomer was isolated, and the yield was nearly quantitative. The quaternary salt (VIIIa), prepared from it by the action of dimethyl sulfate, differs in absorption spectrum (Fig. 3) and melting and decomposition points from the isomeric salt (IXa) obtained by the reaction



Hence, it must have the structure of 1-phenyl-10-ethylphenazinone-3 (VIII).

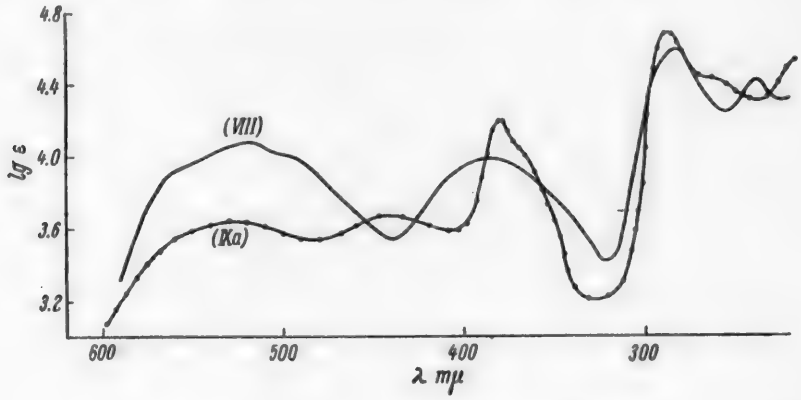
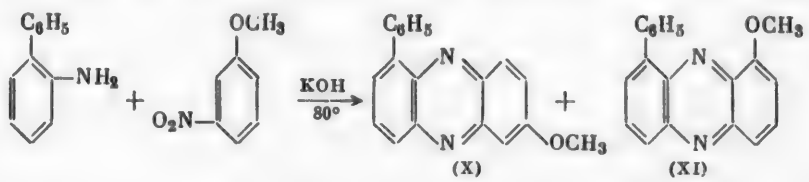
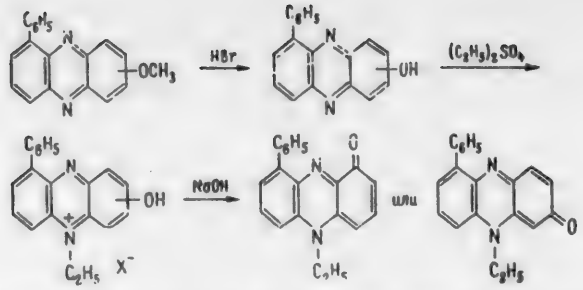


Fig. 3. Absorption spectra in alcohol of (VIII) (3×10^{-5} mole/liter) and (IXa) ($2.5 \times 10^{-5} - 10^{-4}$ mole/liter).

The 1-phenyl-6-methoxyphenazine (X) needed for comparison was prepared, together with its isomer, 1-phenyl-8-methoxy-phenazine (XI), from 2-aminodiphenyl and m-nitroanisole by alkaline condensation in benzene:

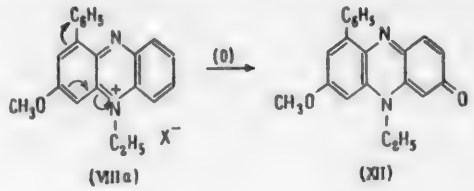


The isomers were separated by chromatography on alumina. From the second zone of the chromatogram was isolated a product with m.p. 203°, and from the fourth zone a product with m.p. 193°. The problem of which isomer corresponded to structure (X) and which to structure (XI) was solved by transforming them into the respective phenazinones by the scheme:



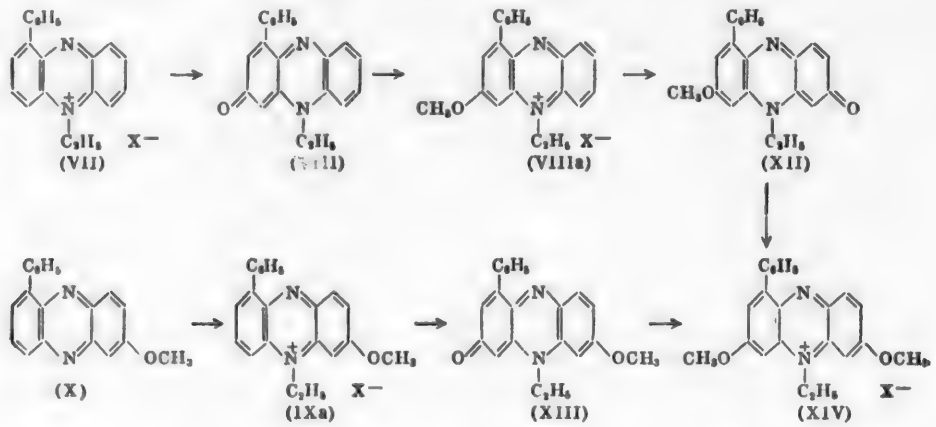
The isomer with m.p. 203° led to formation of 1-phenyl-10-ethylphenazinone-8 (blue color) which could only have been formed from (XI). The second isomer (with m.p. 193°) gave 1-phenyl-10-ethylphenazinone-6 (red color) which must have been derived from 1-phenyl-6-methoxyphenazine (X).

The prepared quaternary salt (VIIIa) is susceptible to further oxidation only in position 6.



(VIIIa) (XII)

However, oxidation in position 6 goes with very much greater difficulty than in position 3. This is easily explained on the basis of the two-sided transfer of electrons from the 6 position to the phenyl group and to the cationic center of the pyrazine ring. 1-Phenyl-3-methoxy-10-ethylphenazinone-6 (XII) has m.p. 254° and four absorption maxima in alcohol at 240, 275, 410, and 520 mμ; it differs markedly from the isomeric 1-phenyl-6-methoxy-10-ethylphenazinone-3 (XIII). Both of the isomers (XII) and (XIII) were treated with dimethyl sulfate and converted into the same substance—1-phenyl-3,6-dimethoxy-10-ethylphenazonium perchlorate (XIV). Transformations by direct and reverse synthesis are represented by the following scheme:



Consequently, in the molecule of a quaternary salt of 1-phenylphenazine, the C_6H_5 group at first directs the oxidation process to the same benzene ring, and subsequently the second benzene ring undergoes oxidation. Oxidation of the second ring is slower than that of the first.

Aryl- and arylalkoxyphenazonium ethosulfates were oxidized under standard conditions. A solution of potassium ferricyanide was stirred into an aqueous solution of the quaternary phenazine salt, followed dropwise by NaOH solution. A red precipitate of the phenazinone-3 usually came down 2-3 min after the start of oxidation, and the entire oxidation process was completed in the course of 1-1.5 hr. The phenazinone-3 precipitate separated as an amorphous solid. The phenazinone-6 came down as a red, viscous mass which slowly solidified. In chromatographic treatment of the phenazinones the following distribution of the zones was usually observed: the

lower zone, containing minute amounts of substance and colored pale-yellow, was the base resulting from decomposition of the quaternary salt of the arylphenazine; in the second zone, narrow and with a blue-violet color, was an insignificant amount of pigment which we did not investigate due to the very small amount. In the third zone, occupying nearly one-half of the chromatographic column, was the phenazinone. Arylphenazinones-3 are characterized under the quartz lamp by a dark-red luminescence and are easily distinguished from arylphenazinones-6 which have a dark-orange luminescence. Some brown dirt collected in a narrow band at the top of the column.

Our numerous attempts at photochemical oxidation of quaternary salts of 1- and 2-phenylphenazine were unsuccessful.

EXPERIMENTAL

2-Phenyl-10-ethylphenazonium perchlorate. A solution of 2.6 g of phenylphenazine in 2 ml of hot nitrobenzene was prepared, 3.5 ml of diethyl sulfate was added, and the mixture was heated for 1.5 hr at 130-140°. The color turned red-brown towards the end of the reaction. The nitrobenzene and diethyl sulfate were washed out with benzene and ether. The quaternary salt forms a dark-red, viscous mass. Yield 4 g (98%). The ethosulfate was converted to the perchlorate for analysis. Golden spangles with m.p. 218-219° (decomp.), crystallizing from 50% alcohol. Absorption maxima in alcohol at 276, 419 mμ.

Found %: N 7.20, 7.38; Cl 9.18, 9.31. $C_{20}H_{17}O_4N_2Cl$. Calculated %: N 7.28; Cl 9.23.

2-Phenyl-10-ethylphenazinone-3 (I). Into a solution of 4 g of 2-phenyl-10-ethylphenazonium ethosulfate in 50 ml of water were stirred 80 ml of 10% potassium ferricyanide solution and 20 ml of 10% sodium hydroxide. After 30 min the deposited phenazinone was filtered, washed with water, and dried in the air. It was purified by chromatography on alumina from benzene. Yield 2.65 g (91%). Red needles, soluble in alcohol, chloroform, and dichloroethane, sparingly soluble in water. M.p. 175°. Absorption maxima in alcohol at 242, 292, 377, and 530 mμ.

Found %: N 9.38, 9.37. $C_{20}H_{16}ON_2$. Calculated %: N 9.33.

2-Phenyl-3-methoxy-10-ethylphenazonium perchlorate (III). Dropwise addition of 1.5 ml of dimethyl sulfate in the course of an hour was made to a boiling solution of 0.5 g of (I) in 25 ml of toluene. Towards the end of the reaction the bright-red solution became orange. The quaternary salt, after cooling, was filtered off, dissolved in 25 ml of water, treated with active carbon, and precipitated with sodium perchlorate. Yield 0.08 g (11%). Bright-orange needles with m.p. 248°, decomp. p. 257°. Absorption maxima in alcohol at 270, 286, 448 mμ. The salt dissolved in concentrated sulfuric acid to form a bright-violet double salt with an absorption maximum at 540 mμ.

Found %: Cl 8.50, 8.55. $C_{21}H_{19}N_2O_5Cl$. Calculated %: Cl 8.56.

2-Phenyl-6-methoxy-10-ethylphenazonium perchlorate (IV). Prepared from 2.9 g of 2-phenyl-6-methoxyphenazine by heating in nitrobenzene at 130-135° for 1.5 hr with 3.5 ml of diethyl sulfate. Crystals of the quaternary salt came down from the hot solution towards the end of the reaction. Yield 4.3 g (99%). The perchlorate forms orange plates with m.p. 223° decomp. p. 233°, crystallizing from 50% alcohol. Absorption maxima at 288, 398, and 485 mμ.

Found %: N 6.74, 6.67; Cl 8.48, 8.46, 8.34. $C_{21}H_{19}O_5N_2Cl$. Calculated %: N 6.75; Cl 8.56.

2-Phenyl-3-methoxy-10-ethylphenazinone-6 (V). Into a solution of 2.8 g of 2-phenyl-3-methoxy-10-ethylphenazonium ethosulfate in 200 ml of water were stirred a solution of 8 g of potassium ferricyanide in 100 ml of water and (dropwise in the course of 1.5 hr) 20 ml of 10% NaOH. The reaction was completed by stirring of the solution for another 3 hr at room temperature. The phenazinone (a red oil) was extracted with chloroform and chromatographed on alumina. From the second zone was isolated 1.7 g (77%) of pure 2-phenyl-3-methoxy-10-ethylphenazinone-6. Red needles from o-xylene, m.p. 238°. Absorption maxima in alcohol at 278, 287, 387, and 526 mμ.

Found %: N 8.65, 8.44. $C_{21}H_{18}O_2N_2$. Calculated %: N 8.50.

2-Phenyl-3,6-dimethoxy-10-ethylphenazonium perchlorate (VI). In the course of 0.5 hr, 2 ml of dimethyl sulfate was introduced dropwise into a boiling solution of 1.3 g (V) in 20 ml of o-xylene. The product was worked

up as for (III). Yield 1.2 g (68%). The perchlorate formed orange needles with m.p. 224°, decomp. p. 232-234°. Crystallized from 50% alcohol and no depression of melting point in admixture with (VIa). Absorption maxima in alcohol at 287, 399, 452 mμ.

Found %: Cl 8.26, 8.39. $C_{22}H_{21}O_6N_2Cl$. Calculated %: Cl 8.00.

2-Phenyl-6-methoxy-10-ethylphenazinone-3 (Va). Prepared similarly to (I) from 4.3 g of 2-phenyl-6-methoxy-10-ethylphenazonium ethosulfate in 90% yield. Dark-red spangles with a bronzy luster, m.p. 182°, crystallizes from toluene. Soluble in benzene and chloroform, partly soluble in ether, insoluble in water. Absorption maxima in alcohol at 240, 302, 366, and 530 mμ.

Found %: N 8.61, 8.43, 8.37. $C_{21}H_{18}O_2N_2$. Calculated %: N 8.48.

2-Phenyl-3,6-dimethoxy-10-ethylphenazonium perchlorate (VIa). To 0.7 g of 2-phenyl-6-methoxy-10-ethylphenazinone-3 in 50 ml of boiling toluene was added 1.5 ml of dimethyl sulfate quickly. Boiling was continued for 2 hr. The salt was filtered and washed with toluene and ether. Yield 0.85 g (88%). Brown needles. The perchlorate formed orange needles with m.p. 224°, decomp. p. 235°. Crystallized from alcohol. Absorption maxima in alcohol at 289, 398, 453 mμ. A mixture with (VI) melted without depression.

Found %: N 6.27, 6.31. $C_{22}H_{21}O_6N_2Cl$. Calculated %: N 6.29.

1-Phenyl-10-ethylphenazonium perchlorate (VII). 2.6 g of 1-phenylphenazine was dissolved in 2 ml of hot nitrobenzene, 3.5 ml of diethyl sulfate was added, and the mixture heated for 1.5 hr at 130-140°. The nitrobenzene and diethyl sulfate were extracted with benzene and ether. Red needles with m.p. 208°, decomp. p. 219°. Absorption maxima in alcohol at 247, 267, 388, and 482 mμ.

Found %: N 7.37, 7.38; Cl 9.26, 9.34. $C_{20}H_{17}O_4N_2Cl$. Calculated %: N 7.28; Cl 9.23.

1-Phenyl-10-ethylphenazinone-3 (VIII). Into a solution of 4 g of 1-phenyl-10-ethylphenazinium in 50 ml of water were stirred 80 ml of 10% solution of potassium ferricyanide and 20 ml of 10% NaOH. After 1.5 hr, the precipitate of phenazinone was filtered, washed with water and dried in the air. Yield nearly quantitative. The product was purified by chromatography over alumina. The isomeric phenazinone-6 was not detected on the chromatogram. M.p. 226°. Dark-red needles. Crystallizes from toluene. Readily soluble in alcohol and chloroform, insoluble in water. Absorption maxima in alcohol at 240, 282, 388 and 522 mμ.

Found %: N 9.32, 9.40. $C_{20}H_{16}ON_2$. Calculated %: N 9.33.

1-Phenyl-3-methoxy-10-ethylphenazonium perchlorate (VIIIa). Prepared by the method described for (III) from 0.5 g of (VIII) in a yield of 0.65 g (93%). Orange needles with m.p. 190°, decomp. p. 230°. Absorption maxima in alcohol at 224, 272, 401, and 475 mμ.

Found %: N 6.97, 7.11; Cl 8.72, 8.71. $C_{21}H_{19}O_5N_2Cl$. Calculated %: N 6.75; Cl 8.56.

1-Phenyl-3-methoxy-10-ethylphenazinone-6 (XII). Prepared similarly to (VIII) from 2.6 g of (VIIIa) in 200 ml of water, 8 g of potassium ferricyanide in 80 ml of water, and 20 ml of 10% NaOH in the course of 3.5 hr. The precipitated phenazinone was filtered and chromatographed on alumina from chloroform. Two layers were distinguished on the chromatogram: a large lower layer (red), eluted by chloroform; a brown upper layer, not eluted by chloroform. Complete evaporation of solvent from the lower layer left 1.4 g (70%) of dark-red needles with m.p. 254° (decomp.). Absorption maxima in alcohol at 240, 275, 410, and 520 mμ.

Found %: N 8.39, 8.53. $C_{21}H_{18}O_2N_2$. Calculated %: N 8.48.

1-Phenyl-3,6-dimethoxy-10-ethylphenazonium perchlorate (XIV). Prepared from 1.4 g of (XII) or (XIII) in 250 ml of toluene and 1.5 ml of dimethyl sulfate by boiling for 1.5 hr. Yield 1.6 g (84%). Orange plates with m.p. 195°, decomp. p. 226-228°. Absorption maxima in alcohol at 286, 391, 429 and 500 mμ.

Found %: N 6.47, 6.52; Cl 7.95, 8.08, 8.15. $C_{22}H_{21}O_6N_2Cl$. Calculated %: N 6.29; Cl 8.00.

1-Phenyl-6-methoxyphenazine (X) and 1-phenyl-8-methoxyphenazine (XI). o-Aminodiphenyl (42 g), m-nitroanisole (38 g) and KOH powder (60 g) were boiled for 20 hr in 250 ml of benzene. The benzene solution was decanted, and the solid residue extracted 3 times with hot benzene (100 ml each time). The benzene solutions were combined and washed with water; volatile substances were distilled off with steam. The residue was dried and chromatographed from benzene on alumina. The second layer of the chromatogram (counting from the bottom) yielded 1.9 g (2.7%) of 1-phenyl-8-methoxyphenazine (XI) in the form of yellow crystals, m.p. 203° (from benzene). Absorption maxima in alcohol at 267, 364, and 470 mμ.

Found %: N 9.87, 9.75. $C_{19}H_{14}ON_2$. Calculated %: N 9.79.

1-Phenyl-8-hydroxyphenazine and 1-phenyl-10-methylphenazinone-8. A mixture of 0.29 g of (XI) and 3 ml of 60% hydrobromic acid was heated in a sealed tube for 4 hr at 150-160°. The content of the tube was extracted with 10% NaOH and filtered from insolubles; the phenazinol was precipitated by acidification of the solution with acetic acid. Yield 0.15 g (55%). Without further purification, the yellow amorphous powder was converted to a quaternary salt by heating with dimethyl sulfate on an oil bath at 130-140° for 30 min. The quaternary salt was extracted from the melt with hot water, filtered, and treated with a few drops of dilute NaOH. Water-insoluble 1-phenyl-10-methylphezaninone-8 came down. Yield 0.03 g (18%). Blue-green needles with m.p. 135° and with an absorption maximum in alcohol at 724 mμ and in acid at 546 mμ. The phenazinone is soluble in alcohol and ether to blue-green solutions.

1-Phenyl-6-methoxyphenazine-10-oxide and 1-phenyl-6-methoxyphenazine (X). The substances isolated in the chromatogramming of the products of condensation of o-aminodiphenyl with m-nitroanisole included (in the fourth layer from the bottom) 5.5 g (7.7%) of 1-phenyl-6-methoxyphenazine-10-oxide in the form of small yellow needles; m.p. 193°, decomp. p. 210°; absorption maxima of the oxide at 276, 370 (inflection), 385, 420, and 444 mμ.

Found %: N 9.02, 8.95. $C_{19}H_{14}O_2N_2$. Calculated %: N 9.27.

Reduction of the oxide with iron filings in acetic acid solution gave 1-phenyl-6-methoxyphenazine (X). Yellow needles with m.p. 182°. Crystallizes from benzene.

Found %: N 9.77, 9.52. $C_{19}H_{14}ON_2$. Calculated %: N 9.79.

1-Phenyl-6-methoxy-10-ethylphenazonium perchlorate. A solution of 0.29 g of 1-phenyl-6-methoxyphenazine in 0.5 ml of nitrobenzene was prepared; 1 ml of dimethyl sulfate was added and the mixture heated for 1 hr at 130-135°. Impurities were extracted with benzene and ether after cooling. Yield 0.35 g (80%). Crystallizes from 50% alcohol. Brown-red needles with m.p. 228° (decomp.). Easily oxidized to red phenazinone. Absorption maxima of the quaternary salt in alcohol at 260 (diffuse), 287, 380, 445, and 530 mμ.

Found %: N 6.85, 6.86; Cl 8.60, 8.82. $C_{21}H_{19}O_5N_2Cl$. Calculated %: N 6.75; Cl 8.56.

10-Oxide of 1-phenyl-6-methoxy-9-methylphenazonium perchlorate. 0.3 g of 1-phenyl-6-methoxyphenazine-10-oxide was dissolved in 1 ml of hot nitrobenzene, 1.5 ml of dimethyl sulfate was added at 130-135°, and heating was continued at the same temperature for half an hour. Impurities were extracted with benzene and ether after cooling. Yield of perchlorate 0.3 g (71%). Orange plates with m.p. 206° (decomp.). Crystallizes from alcohol. Absorption maxima at 260, 371 and 390-420 (inflection) mμ.

Found %: N 6.72, 6.73. $C_{20}H_{17}O_6N_2Cl$. Calculated %: N 6.72.

1-Phenyl-10-ethylphenazinone-6. A mixture of 0.72 g of 1-phenyl-6-methoxyphenazine and 3 ml of 60% hydrobromic acid was heated for 4 hr in a sealed tube at 150-160°. The reaction product was extracted from the test tube and dissolved in 10% NaOH; the solution was filtered from insolubles and acidified with acetic acid. 1-Phenyl-6-hydroxyphenazine came down and was washed with water and dried. Yield 0.32 g (47%). The product was sufficiently pure for transformation into the quaternary salt and subsequently into the phenazinone without special purification. Conversion to the quaternary salt was effected by heating for 2 hr with 1 ml of diethyl sulfate; after cooling, impurities were extracted with benzene and ether; 1-phenyl-6-hydroxy-10-ethylphenazonium ethosulfate was extracted with 5 ml of water and treated with a few drops of 2% NaOH. Yield 0.11 g (14%). M.p. 204°.

Found %: N 9.25, 9.18. $C_{20}H_{16}ON_2$. Calculated %: N 9.33.

SUMMARY

Spectral data and the results of syntheses and reverse syntheses showed that in the oxidation of quaternary salts of 1- and 2-phenylphenazines, the C_6H_5 group directs the oxidation process at first to the benzene ring containing the substituent, but later the second ring undergoes oxidation. New quaternary salts and N-alkylphenazinones containing phenyl and methoxy groups in the benzene rings of phenazine were obtained; their absorption spectra were investigated.

LITERATURE CITED

[1] H. Mc Ilwain, J. Chem. Soc. 1704 (1937); S. B. Serebryanyi, Uspekhi Khim. 24, 331 (1955).

[2] A. I. Kiprianov and M. M. Kroshchenko, Ukr. Khim. Zhur. 22, 551 (1956).

[3] S. B. Serebryanyi, Zhur. Obshchei Khim. 22,2203 (1952)*; Ukr. Khim. Zhur. 23, 358 (1957); Yu. S. Rozum, Zhur. Obshchei Khim. Coll. I, 600 (1953).

[4] V. G. Shaposhnikov, Investigations on Azine and Azonium Dyes [in Russian] (Kiev, 1904).

*Original Russian pagination. See C. B. translation.

ULTRAVIOLET ABSORPTION SPECTRA OF 2-METHYLBENZOTHIAZOLES CONTAINING UNSATURATED SUBSTITUENTS IN POSITIONS 5 AND 6

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4045-4048,

December, 1959

Original article submitted November 21, 1958

In the preceding communications [1-3] we described derivatives of benzothiazole containing unsaturated substituents in positions 5 and 6, as well as various cyanine dyes prepared from these bases. In connection with the establishment of the fine structure of the synthesized dyes (clarification of the nature of the secondary chromophores and their influence on absorption), interest is attached to a study of the ultraviolet absorption spectra of the original heterocyclic bases. In this communication we submit the results of an investigation of the absorption spectra* of alcoholic solutions of derivatives of 2-methylbenzothiazole containing styryl, p-methyl-, p-methoxy, p-nitrostyryl, and γ-phenylbutadienyl groups in positions 5 or 6.

Absorption spectra of benzothiazole and of a series of its derivatives have been described in the literature [4-11]. Lutskii [4] and Kiprianov [5] report two absorption bands for 2-methylbenzothiazole, and the former observed a fine structure of the band in the region of longer waves (λ_{max} 2915, 2825, 2535 A [4]). We find for 2-methylbenzothiazole (Fig. 1, II) one additional band of great intensity at 218 mμ.

The absorption curve of 2-methyl-6-styrylbenzothiazole (III) is plotted in Fig. 1. Bands 1 and 2 of 2-methylbenzothiazole are still present and are more intense. In addition, there is a strong band at 311 mμ. The latter may be associated with the presence of a new chromophoric system involving the styryl group. This chromophore evidently belongs to the stilbene radical linked to the thiazole ring, due to which the stilbene band (Fig. 1, I [12]) is shifted to longer wavelengths. The 311 mμ band actually disappears when the conjugation is destroyed by addition of bromine to the double bond of the styryl group.

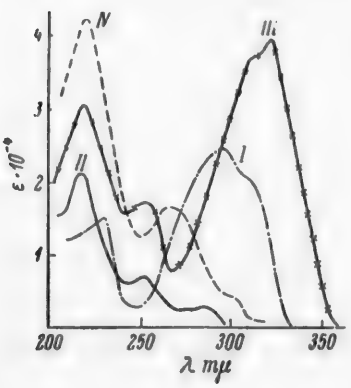


Fig. 1.

Absorption spectra of five derivatives of 2-methylbenzothiazole containing unsaturated groups in position 6 are plotted in Fig. 2. Positions of the bands and the extinctions are set forth in the table. The absorption curve of 2-methyl-6-styrylbenzothiazole is included in Fig. 2 for comparison.

We see from Fig. 2 that all of the bases exhibit three well-marked bands, but these differ in position and intensity according to the nature of the substituent in the para-position of the styryl group and the length of the conjugated chain of the unsaturated radical. Some curves (I, IV, V) are inflected and possess an additional absorption maximum (curve V).

The long-wave bands of the investigated bases, which belong to chromophores associated with unsaturated substituents, are within the 321-365 mμ region. Introduction into the para-position of the styryl radical of both electron-donating and electron-accepting

*Measurements with a SF-4 spectrophotometer.

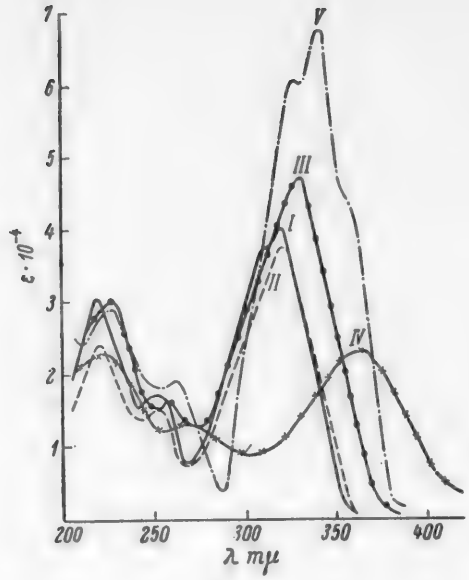


Fig. 2.

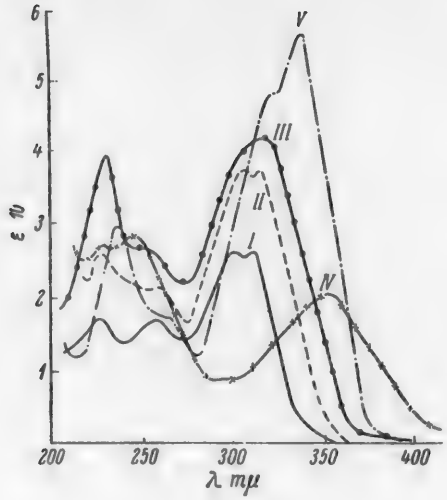
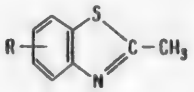


Fig. 3.

substituents causes band 3 to be shifted to longer wavelengths. Lengthening of the conjugated chain of the styryl radical by introduction of one vinylene group (Fig. 2, V) also causes a bathochromic shift of band 3. The intensity of this band in the case of bases containing electron-donating substituents in the para-position of the styryl radical hardly changes (II) or increases slightly (III), while introduction of a nitro group (IV) reduces the intensity. Transition from a styryl-substituted to a vinylene homolog—γ-phenylbutadienyl-substituted—markedly increase the intensity of band 3 (V).

TABLE



Derivatives of 2-Methylbenzothiazole

Fig. no.	Curve no.	R	Substituent position	Absorption maximum (in mμ)			ε · 10⁻⁴		
				1	2	3	1	2	3
1	II	H	—	218	252	283	2.10	0.70	0.25
1	III	$C_6H_5CH=CH$	6	219	252	321	3.07	1.72	3.97
2	II	$p\text{-}CH_3C_6H_4CH=CH$	6	220	252	324	2.42	1.52	3.75
2	III	$p\text{-}CH_3OC_6H_4CH=CH$	6	228	257	332	3.00	1.65	4.65
2	IV	$p\text{-}NO_2C_6H_4CH=CH$	6	223	268	364	2.25	1.30	2.30
2	V	$C_6H_5(CH=CH)_2$—	6	227	262	344 * (329)	2.90	1.90	6.67 (6.00)
3	I	$C_6H_5CH=CH$—	5	226	256	312 (301)	1.72	1.70	2.6 (2.62)
3	II	$p\text{-}CH_3C_6H_4CH=CH$	5	227	258	315 (307)	2.62	2.15	3.80 (3.80)
3	III	$p\text{-}CH_3OC_6H_4CH=CH$	5	230	254 inflection	318	4.00	—	4.20
3	IV	$p\text{-}NO_2C_6H_4CH=CH$	5	229	245	354	2.75	2.86	2.05
3	V	$C_6H_5(CH=CH)_2$	5	237	263 inflection	337	3.00	—	5.66
1	IV	$C_6H_5CHBrCHBr$—	6	220	266	302 inflection	4.25	1.65	—

* Additional short-wave absorption maximum in brackets.

It is interesting to note that the regularities of displacement of the long-wave bands and the changes in their extinctions also apply to the corresponding 5-derivatives of 2-methylbenzothiazole (Fig. 3), although the absorption bands of the latter are at much shorter wavelengths and the extinctions are slightly smaller than those of the 6-substituted derivatives (see the table).

SUMMARY

A study was made of the absorption spectra of ten derivatives of 2-methylbenzothiazole containing unsaturated substituents in the benzothiazole nucleus. Introduction of unsaturated substituents is found to develop a strong absorption band in the long-wave region. This band is nearer the red end of the spectrum in the case of 6-derivatives than in the case of 5-derivatives of 2-methylbenzothiazole.

LITERATURE CITED

[1] I. K. Ushenko and S. E. Gornostaeva, Zhur. Obshchei Khim. 28, 1668 (1958).*

[2] M. A. Al'perovich, I. K. Ushenko, and L. N. Tyurina, Zhur. Obshchei Khim. 28, 2538 (1958).*

[3] M. A. Al'perovich, I. K. Ushenko, and L. N. Tyurina, Zhur. Obshchei Khim. 29, 3606 (1959).*

[4] A. E. Lutskii and I. A. Sidorov, Zhur. Obshchei Khim. 17, 141 (1947).

[5] A. I. Kiprianov and Yu. S. Rozum, Zhur. Obshchei Khim. 21, 2038 (1951).*

[6] A. I. Kiprianov and V. E. Petrun'kin, Zhur. Obshchei Khim. 10, 622 (1940).

[7] W. Boggust and W. Cocker, J. Chem. Soc. 358 (1949).

[8] A. I. Kiprianov and V. A. Shrubovich, Zhur. Obshchei Khim. 26, 2891 (1956).*

[9] A. I. Kiprianov and I. P. Fedorova, Ukr. Khim. Zhur. 21, 76 (1955).

[10] A. I. Kiprianov and I. P. Fedorova, Ukr. Khim. Zhur. 23, 59 (1957).

[11] A. I. Kiprianov and I. P. Fedorova, Zhur. Obshchei Khim. 28, 1023 (1958).*

[12] R. N. Beale and E. M. Roe, J. Chem. Soc. 2755 (1953); T. Forster, Uspekhi Khim. 9, 86 (1940).

*Original Russian pagination. See C. B. translation.

RADICAL EXCHANGE IN ORGANOMETALLIC COMPOUNDS

II. EXCHANGE BY PHENYL AND ETHYL RADICALS IN ORGANOMAGNESIUM COMPOUNDS

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Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4048-4051,

December, 1959

Original article submitted December 7, 1958

Exchange of radicals in solutions is of great interest from the aspect of understanding of the mechanism of various chemical processes. The study of exchange reactions by radicals in organometallic compounds is extremely important. In previous communications [1, 2] we studied the possibility and the conditions of radical exchange in some organic compounds of mercury and lead. Susceptibility of Grignard reagent radicals to exchange has been reported in the literature [3, 4]. Following up our earlier work [1] on the occurrence of radical exchange in organomagnesium compounds, we have now carried out more detailed experiments in this field.

In the present work we studied exchange by phenyl and ethyl radicals in the systems phenylmagnesium bromide—bromobenzene in ether, phenylmagnesium bromide—benzene in ether and in dimethylaniline, and ethylmagnesium bromide—ethyl bromide in ether and in dimethylaniline. The benzene, bromobenzene and ethyl bromide were labeled with radiocarbon C^{14}.

EXPERIMENTAL*

Ethyl bromide labeled with C^{14} was prepared by bromination of 1-C^{14}-ethanol. We synthesized the latter by the Grignard reaction from methylmagnesium iodide and labeled carbon dioxide [5]. Bromobenzene labeled with C^{14} was prepared by bromination of radioactive benzene, which we synthesized from labeled acetylene [6], in turn prepared from labeled barium carbide [7].

TABLE 1

Experiments on Exchange by Phenyl Radicals Between Phenylmagnesium Bromide and Labeled Bromobenzene in Ether

Expt. no.	Reaction conditions (temperature, uv irradiation)	Time, hr	Activity (pulses/min)			Exchange %
			calc. for 100% exchange	of Grignard reagent after exchange	of secondary products	
1		100	140	—	106 (diphenyl)	—
2	Irradiation with mercury vapor lamp	100	182	—	152 (diphenyl)	—
3	40°	12	12000	—	920 (benzene)	—
4	80	12	12000	—	1106 (benzene)	—

* V. K. Sukhotin and V. A. Savin took part in the experimental work.

Equimolar quantities (in terms of radicals) of Grignard reagent and benzene or bromobenzene were placed in a quartz test tube fitted with a ground-glass stopper and a vacuum tap. The tube was immersed in liquid nitrogen and pumped out with a forevacuum pump. The vacuum tap was then closed. The tube was irradiated with ultraviolet light from a mercury-vapor lamp for 30 to 100 hr. Quantitative determination of the Grignard reagent was performed by the method described by Gilman et al. [8].

In experiments with application of heat, the radical-equimolar quantities of components were placed in a pyrex ampoule. This was immersed in liquid nitrogen, pumped out with a forevacuum pump, and sealed. It was then placed in a glycerol thermostat at the required temperature for 12 hr. The ampoule was then opened. The reaction mas was carboxylated with solid carbon dioxide and decomposed with hydrochloric acid. Benzoic acid was then isolated (in some experiments also diphenyl).

In experiments with ethylmagnesium bromide the carboxylation of the reaction mixture with solid carbon dioxide for the purpose of separation of reaction products was ineffective due to the difficulty of isolation of propionic acid or its salt because the latter were formed in too small quantity. The reaction mixture was therefore decomposed with acified water. The resulting ethane was purified from possible traces of ethyl bromide by passage in succession through traps containing alcohol, concentrated alkali solution, and concentrated sulfuric acid. It was then collected in a gas separator. Special preliminary experiments showed that this procedure for elimination of possible traces of labeled ethyl bromide was fully reliable if the gas was passed slowly through the traps. The reaction products were subjected to radiometric analysis in an internally filled counter [2] with an accuracy of ± 2%. Gaseous products were subsequently examined by qualitative and quantitative chromatographic analysis.

Exchange by phenyl radicals does not take place in the system phenylmagnesium bromide–bromobenzene. In experiments 1 and 2 (Table 1), diphenyl containing about 40% of the activity of the original bromobenzene was isolated. The existing experimental data indicate the presence of free phenyl radicals during the reaction. If this conclusion is correct, then labeled benzene must have been formed as one of the reaction products, as a result of interaction of the phenyl radical with the solvent [9, 10]. We ran special experiments to check this theory, using bromobenzene of relatively high activity as starting substance, since the quantity of benzene formed in the course of the reaction may be very minute. After the exchange reaction had been carried out, unlabeled benzene was added to the reaction mixture. Radiochemical analysis of the benzene collected during fractional distillation of the reaction mixture revealed the presence of activity in the benzene (experiments 3 and 4, Table 1).

TABLE 2

Exchange of Phenyl Radicals Between Phenylmagnesium Bromide and Labeled Benzene

Solvent	Reactions conditions (temperature, uv irradiation, catalyst)	Time	Activity (pulses/min)		Exchange %
			calculated on 100% exchange	of Grignard reagent after exchange	
Ether	Hg-vapor lamp	80	204	—	—
	ditto, $FeCl_3$	30	204	—	—
	ditto, $AlBr_3$	30	204	—	—
	20°	12	402	—	—
	40	12	1500	57	3.8
	60	12	1500	65	4.3
	80	12	1500	79	5.2
Dimethylaniline	40	12	1500	44	3.0
	60	12	1500	63	4.2
	80	12	1500	70	4.7

In experiments on exchange between phenylmagnesium bromide and benzene (Table 2) the exchange found is within the limit of experimental error and amounted to 3-5%. This is consistent with the data of other authors [11]. Replacement of ether by a more strongly polar solvent (dimethylaniline) did not increase the percentage of exchange.

In the system ethylmagnesium bromide–ethyl bromide, complete exchange was detected and equilibrium was established (Table 3). Exchange is 30% in Expt. 4 (Table 3) at 60°, and rise of temperature to 80° also leads to complete exchange.

Chromatographic analysis of the gas collected from the reaction ampoule (about 70 ml), still before decomposition of the reaction mixture, showed the presence of 48.6% of ethane, 47.5% of ethylene, and 3.9% of butane. Therefore, in the course of the exchange reaction in the system (whose mechanism must be clarified by further study) free ethyl radicals are formed and disproportionate to give ethane and ethylene; some of the radicals also dimerize to form butane.

TABLE 3

Exchange by Ethyl Radicals Between Ethylmagnesium Bromide and Labeled Ethyl Bromide

Expt. no.	Solvent	Reaction conditions t (°C)	Time	Activity (pulses/min) calculated on 100% exchange	Activity (pulses/min) of Grignard reagent after exchange	Exchange%
1	Ether	40°	12	2510	2480	98.8
2		60	12	2510	2428	96.7
3		80	12	2510	2460	98.0
4	Dimethylaniline	60	12	2510	915	36.4
5		80	12	2510	2497	99.5

We also carried out experiments on radical exchange in the systems ethylmagnesium bromide–benzene and phenylmagnesium bromide–ethyl bromide. No exchange occurs in the system ethylmagnesium bromide–benzene, and we did not isolate benzoic acid. Exchange occurred in the system phenylmagnesium bromide–ethyl bromide, as demonstrated by the isolation of C^{14}-labeled ethane after decomposition of the reaction mixture.

SUMMARY

1. Exchange by phenyl and ethyl radicals in organomagnesium compounds was studied.

2. Exchange by phenyl radicals between phenylmagnesium bromide and bromobenzene or benzene either does not occur at all or only to an extent within the limits of experimental error.

3. Complete exchange by ethyl radicals between ethylmagnesium bromide and ethyl bromide was observed.

LITERATURE CITED

[1] I. A. Korshunov, R. V. Amenitskaya, A. A. Orlova, and A. P. Batalov, Zhur. Obshchei Khim. 29, 1992 (1959).*

[2] I. A. Korshunov and A. P. Batalov, Zhur. Obshchei Khim. 29, 3135 (1959).*

[3] M. F. Shostakovskii and M. R. Kulibekov, Zhur. Obshchei Khim. 28, 578 (1958).*

[4] M. F. Shostakovskii and M. R. Kulibekov, Zhur. Obshchei Khim. 28, 951 (1958).*

[5] M. B. Neiman and G. I. Feklisov, Doklady Akad. Nauk SSSR 87, 605 (1952).

[6] A. A. Korotkov and S. P. Mitsengendler, Izvest. Akad. Nauk SSR, Otdel. Khim. Nauk 1509 (1956).*

[7] N. P. Keier, B. V. Klimenok, and G. V. Isagulyants, Doklady Akad. Nauk SSSR 85, 1029 (1952).

[8] H. Gilman, P. D. Wilkinson, W. P. Tishel, and G. H. Mevers, J. Am. Chem. Soc. 45, 150 (1923).

[9] G. A. Razuvaev and Yu. A. Ol'dekop, Zhur. Obshchei Khim. 19, 736 (1949).*

[10] G. A. Razuvaev and Yu. A. Ol'dekop, Zhur. Obshchei Khim. 19, 1483 (1949).*

[11] G. A. Razuvaev, G. G. Petukhov, M. A. Shubenko, and V. A. Voitovich, Ukr. Khim. Zhur. 22, 45 (1956).

*Original Russian pagination. See C. B. translation.

SYNTHESES AND TRANSFORMATIONS IN THE DIARYLUREA SERIES

VII. HYDROLYSIS OF HEXACHLORODIPHENYLUREAS

D. F. Kutepov

Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4051-4054,

December, 1959

Original article submitted December 6, 1958

We previously [1, 2] studied the hydrolytic properties of diphenylurea and its nitro and alkoxy derivatives. These compounds were shown to be highly resistant to hydrolysis both in an acid and in an alkaline medium. In the present work we investigated the hydrolytic behavior of 2,2',4,4',6,6'- and 2,2',4,4',5,5'-hexachlorodiphenylureas. Our experiments showed that these compounds have higher resistance to hydrolysis and are susceptible to cleavage only under drastic conditions. The hydrolytic stability of hexachlorodiphenylureas is greatly influenced by the medium (acid or alkaline), the temperature, and the duration of the process. They are relatively easily hydrolyzed in aqueous ammonia solution. A comparative study of the rate of hydrolysis of 4,4'-dinitrodiphenylurea and 2,2',4,4',6,6'-hexachlorodiphenylurea (admixed with much tetra- and pentachloro-substituted diarylureas) showed that the chloro-substituted diarylureas have a greater hydrolytic stability. Heating of the former in 5% aqueous ammonia for 5 hr at 150° under pressure led to a yield of 93% of p-nitroaniline; in the case of the chloro derivative, the total yield of 2,4,6-trichloroaniline and 2,4-dichloroaniline was 83%.

Results are plotted in the figure.

In a study of the hydrolysis of 2,2',4,4',6,6'- and 2,2',4,4',5,5'-hexachlorodiphenylureas in sulfuric acid, we observed slower hydrolysis of the latter. In solution in 90% sulfuric acid at room temperature, 2,2',4,4',5,5'-hexachlorodiphenylurea remains unchanged for 24 hr, whereas under the same conditions 2,2',4,4',6,6'-hexachlorodiphenylurea slowly breaks down to trichloroaniline and carbon dioxide. This difference in behavior is evidently the consequence of the presence in 2,2',4,4',6,6'-hexachlorodiphenylurea of two atoms of chlorine in the ortho-position; this intensifies the inductive effect and weakens the carbamide linkage.

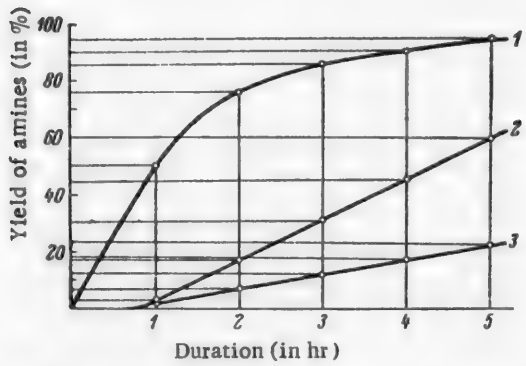
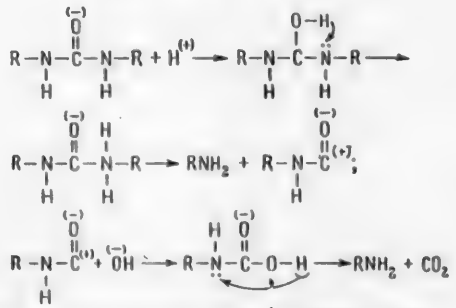


Figure. Yield of amines on hydrolysis of substituted ureas. 1) p-Nitroaniline; 2) 2,4,6-trichloroanilines; 3) 2,4-dichloroaniline.

Hydrolysis of diarylureas follows an ionic mechanism and can be represented by the following scheme:

$$H_2O \rightleftarrows H^+ + OH^-$$



where R = C_6H_5, $C_6H_2Cl_3$, $C_6H_3Cl_2$, $O_2NC_6H_4$, etc.

At higher temperatures, however, it follows another course in accordance, apparently, with the scheme:

$$RNHCONHR \rightleftharpoons RNH_2 + RNCO$$

$$RN{=}C{=}O + H^+ + \bar{O}H \longrightarrow RN(H)-C(=O)-O-H \longrightarrow RNH_2 + CO_2$$

On hydrolysis of the chemically pure compounds under optimum conditions, we obtained quantitative yields of end products—aromatic amines and carbon dioxide (the latter in the form of barium carbonate).

EXPERIMENTAL

1. Hydrolysis of 2,2',4,4',6,6'-hexachlorodiphenylurea in sulfuric acid. a) Hexachlorodiphenylurea (10 g), obtained by chlorination of diphenylurea in an aqueous medium, was mixed with 101.8 g of 85% sulfuric acid. The pasty mass was transferred to a reactor and stirred for 3 hr at 150°. After the precipitate had been removed, the filtrate was poured onto ice. The resulting 2,4,6-trichloroaniline was filtered, washed with water, and dried at 50°. Part of the trichloroaniline was extracted from the precipitate with alcohol, and the alcoholic filtrate treated with water. Yield of trichloroaniline 70%, m.p. 77.5°.

Found %: N 7.02, 7.08. $C_6H_4NCl_3$. Calculated %: N 7.12.

Up to 30% of the original substance was found in the residue after separation of the 2,4,6-trichloroaniline, and this revealed the incomplete hydrolysis of hexachlorodiphenylurea under the conditions described.

b) Hydrolysis of 2,2',4,4',6,6'-hexachlorodiphenylurea in 91% sulfuric acid by heating for 3 hr at 160° gave 2,4,6-trichloroaniline in 98.6% yield; m.p. 76°.

c) A mixture of 200 g of 2,2',4,4',6,6'-hexachlorodiphenylurea and 500 g of 90% sulfuric acid was stood at room temperature for 24 hr. The next day the hexachlorodiphenylurea was filtered off. There were obtained 186 g of the original hexachlorodiphenylurea (m.p. 325°) and 9.2 g of 2,4,6-trichloroaniline with m.p. 77°.

2. Hydrolysis of 2,2',4,4',5,5'-hexachlorodiphenylurea. a) A mixture of 200 g of hexachlorodiphenylurea and 200 g of 90% sulfuric acid was heated for 1.5 hr at 160°. Dilution of the reaction mixture with water led to separation of 182 g (97%) of trichloroaniline with m.p. 96.5°.

b) A mixture of 2,2',4,4',5,5'-hexachlorodiphenylurea and 500 g of 90% sulfuric acid was stood for 24 hr at room temperature. The next day the hexachlorodiphenylurea was filtered and 196 g of the original substance was recovered. No 2,4,5-trichloroaniline was detected when the sulfuric acid was diluted with water.

c) A mixture of 100 g of 2,2',4,4',5,5'-hexachlorodiphenylurea and 200 g of 90% sulfuric acid was slowly heated on a gauze with stirring. Carbon dioxide evolution commenced as soon as the temperature reached 130° and the gas was collected in barytes water. Heating was continued for 3 hr, the temperature gradually rising to 160°. At this point gas evolution ceased, and consequently also the hydrolytic cleavage of the hexachlorodiphenylurea. Dilution of the acid with water led to separation of 91.2 g of trichloroaniline (7.5%). M. p. 96.5°, corresponding to the melting point of 2,4,5-trichloroaniline [3].

The yield of barium carbonate was equivalent to the quantity of carbon dioxide that should have been evolved on hydrolysis of the hexachlorodiphenylurea.

3. Hydrolysis of 2,2',4,4',6,6'-hexachlorodiphenylurea in aqueous ammonia solution. Experiments were performed in a glass-lined autoclave without a stirrer. The material subjected to hydrolysis was hexachlorodiphenylurea obtained by chlorination of diphenylurea with elemental chlorine in an aqueous medium and consisting of a mixture of chlorine-substituted diarlyureas. The reaction was performed in 1500 ml of 5% aqueous ammonia at 150° and a pressure of 7 atm. The reaction mass contained a black deposit which was filtered and distilled with steam. The distilled light-colored product was filtered and dried at 50°. The 2,4,6-trichloroaniline and 2,4-dichloroaniline so obtained were subjected to fractionation by stirring for 10 min at 70° with 5% hydrochloric acid solution (using 150 ml of acid for 100 g of product). We found that the trichloroaniline remains unreacted, while the dichloroaniline forms a water-soluble hydrochloride of adequate stability and goes into solution. The 2,4,6-trichloroaniline was filtered off, washed with water, dried, and recrystallized from al-

cohol; m.p. 76-77°. The filtrate was made alkaline to bring out the 2,4-dichloroaniline, which was then washed with water and dried at 50°; m.p. 66-67° (after recrystallization, m.p. 68° [3]). The experimental results are plotted in the figure.

b) Under the same conditions 10 g of 4,4'-dinitrodiphenylurea was hydrolyzed, and p-nitroaniline with m.p. 148° was obtained. Yields are shown in the diagram.

c) Chemically pure 2,2',4,4',6,6'-hexachlorodiphenylurea (10 g) was heated in 5% aqueous ammonia solution at 150° and 8-10 atm for 3 hr. The yield of 2,4,6-trichloroaniline was 81.9%; m.p. 78°.

4. Hydrolysis of 2,2',4,4',5,5'-hexachlorodiphenylurea in aqueous ammonia solution. Chemically pure hexachlorodiphenylurea (4 g) was hydrolyzed in 40 ml of 5.1% aqueous ammonia in a sealed tube at 170° for 5 hr. The yield of 2,4,5-trichloroaniline was 99.2%; m.p. 96.5°.

SUMMARY

1. Hexachlorodiphenylureas possess high hydrolytic stability and undergo cleavage only under drastic conditions.

2. A mechanism of the process of hydrolysis of diarylureas is proposed.

LITERATURE CITED

[1] I. M. Kogan and D. F. Kutepov, Zhur. Obshchei Khim. 21, 1499, 2028 (1951).•

[2] D.F. Kutepov and Z. G. Bukolova, Zhur. Obshchei Khim. 24, 698 (1954).•

[3] D.F. Kutepov and N. S. Rozanova, Zhur. Obshchei Khim. 26, 1737 (1956);• 27, 1845 (1957).•

• Original Russian pagination. See C. B. translation.

THE SYNTHESIS OF p,p'-DIPHENYLSTILBENE

E. E. Baroni and G. Bushbek

Translated from Zhurnal Obshchei Khimii, Vol. 29, No. 2, pp. 4055-4056,

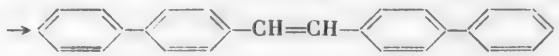
December, 1959

Original article submitted December 16, 1958

In the literature there has appeared a whole series of reports on the successful use of p,p'-diphenylstilbene as a luminescent additive for plastic scintillators based on vinyltoluene [1]. The method of synthesis of this compound, however, is indicated neither in the mentioned work nor in the general literature.

We have devised the following synthesis for p,p'-diphenylstilbene

$$2p\text{-}C_6H_5C_6H_4CHO \longrightarrow p\text{-}C_6H_5C_6H_4CH(OH)COC_6H_4C_6H_5\text{-}p \longrightarrow$$



Diphenyl, which serves as the starting material, is converted into p-phenylbenzaldehyde by the carbonyl reaction [2].

p-Phenylbenzaldehyde undergoes the benzoin condensation, analogous to the condensation of benzaldehyde [3], to produce p,p'-diphenylbenzoin.

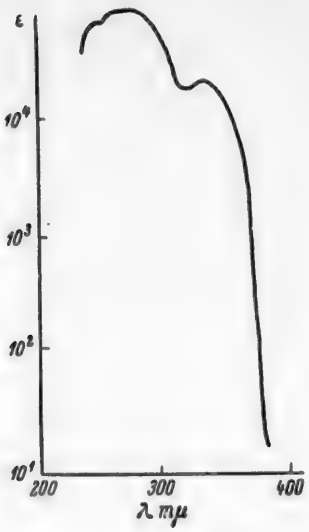
Conversion of p,p'-diphenylbenzoin into p,p'-diphenylstilbene, analogous to the known method of production of stilbene from benzoin [4], does not occur, apparently because of the great steric hindrance involved. Therefore, reduction and dehydration were carried out simultaneously using zinc dust and hydrochloric acid in an atmosphere of hydrogen. The product, p,p'-diphenylstilbene, both in the crystalline form and in organic solvents, exhibits intense blue fluorescence on illumination by ultraviolet light. The structure of the compound was confirmed by its absorption spectrum (see figure) and also by elementary analysis and cryoscopic molecular weight determination.

EXPERIMENTAL

p-Phenylbenzaldehyde. The synthesis was carried out by the described method [2]. Recrystallization from ligroine did not produce a completely pure substance. Rapid vacuum sublimation gave colorless crystals with m. p. 60°.

p,p'-Diphenylbenzoin. A solution of 1 g of sodium cyanide in 10 ml of water was added to 7 g of p-phenylbenzaldehyde dissolved in 70 ml of 96% alcohol, and the mixture heated for two hours on a water bath. A voluminous yellow precipitate was formed, which was filtered off, washed well with 100 ml of 50% alcohol, and dried. There was obtained 6.31 g (90%) of small colorless crystals with m.p. 149-150° (recrystallized from alcohol).

p,p'-Diphenylstilbene. A stream of hydrogen and hydrogen chloride gas was passed through a mixture of 6 g of p,p'-diphenylbenzoin, 4 g of zinc dust, and 75 ml of 96% alcohol while heating the mixture to reflux and stirring vigorously. The gas mixture was generated by the action of concentrated hydrochloric acid on zinc dust. The white flaky mass was gradually converted into a yellow precipitate which separated easily from the alcoholic



Absorption spectrum of p,p'-diphenylstilbene in dioxane (concentration 1 mg/cc)

solution. The reaction took 2.5-3 hours. The mixture was diluted with water, the precipitate filtered off, washed with water, and dried. Excess zinc dust was removed by filtration in hot benzene solution, and the substance was then recrystallized. The product was sublimed in a high vacuum (10^{-4} mm) at 200°C. Faintly green transparent crystals were obtained, m.p. 222-223°, which fluoresced strongly in ultraviolet light. Yield 4.50 g (78.2%).

Found %: C 94.24, 93.87; H 5.91, 6.04. M 339.0 (in diphenyl). $C_{26}H_{20}$. Calc. %: C 93.92; H 6.08. M 332.42.

p,p'-Diphenylstilbene is almost insoluble in all organic solvents.

SUMMARY

A scheme for the synthesis of p,p'-diphenylstilbene has been devised, and two compounds not previously reported in the literature have been isolated: p,p'-diphenylbenzoin, and p,p'-diphenylstilbene.

LITERATURE CITED

[1] R. K. Swank, Nucleonics 12, 14 (1954); J. Fischer, Nucleonics 13, 52 (1955); M. Hyman, Am. Patent 2710284 (1955); J. H. Pannel and B. Manning, J. Chem. Phys. 23, 1368 (1955).

[2] Gattermann, Lieb. Ann. 347, 347 (1906); Hey, J. Chem. Soc. 2476 (1931).

[3] Zincke and Breuer, Lieb. Ann. 198, 151 (1879).

[4] A. Blank, Lieb. Ann. 248, 12 (1888); J. C. Irvine and J. Weir, J. Chem. Soc. 91, 1384 (1907); D.A. Ballard and W. M. Dahn, J. Am. Chem. Soc. 54, 3969 (1932).

THE SYNTHESIS OF 2,4,5-TRICHLOROTHIOPHENYL ESTERS OF N-PHTHALOYLAMINO ACIDS

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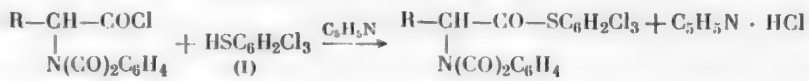
Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4056–4058, December 1959

Original article submitted December 27, 1958

Wieland and co-workers [1] have synthesized thiophenyl esters of amino acids and used them for the synthesis of peptides. The thioesters were prepared by the reaction of mixed anhydrides of carbobenzoxyamino acids and carbonic acids or hydrochlorides of amino acid chlorides [2] with thiophenol. Farrington and co-workers [3] observed racemization during the preparation of thioesters by the mixed anhydride method. They suggested the use of p-nitrothiophenyl esters of acylamino acids in peptide synthesis, which they prepared from tri-(p-nitrophenylthio)-phosphate, as in this way, ammonolysis of the thioester bond occurs very easily without racemization.

In the present communication we report the synthesis of 2,4,5-trichlorothiophenyl esters of N-phthaloylamino acids which we prepared from the appropriate acid chlorides and trichlorothiophenol (I).



The acid chlorides were prepared from the acylamino acids and thionyl chloride (II), and without further purification were reacted with (I) in the presence of pyridine. In this way derivatives of phthaloylalanine (III), phthaloylvaline (IV), phthaloylleucine (V), and phthaloylphenylalanine (VI) were prepared in yields of 61–75%. The thioesters formed in such reactions were isolated as colorless, crystalline substances, sparingly soluble in alcohol, petroleum, and diethyl ether, but readily soluble in ethyl acetate and tetrahydrofuran. On account of the low reactivity of the compounds formed, it was not possible to use them in peptide syntheses. They did not react with esters of amino acids in the presence of bases, even on lengthy standing or heating. The inertness of the thioester bond in trichlorothiophenol esters appears to be associated with the influence of the three chlorine atoms in the aromatic nucleus. Saponification of the esters may be brought about by boiling with 10% alkali. On treatment with hydrazine in either aqueous or alcoholic medium, fission of the -CO-S-bond occurs, and a phthaloyl group is removed, with the formation of the amino acid hydrazide and (I). We studied this reaction for the case of the thioester of phthaloyl-DL-valine (VII) and found that the formation of (I) in alcoholic medium occurs very readily even at room temperature, and is complete in 2–3 hours. After separating the phthaloyl hydrazide, a substance was found in the residue which was identified on a chromatogram as the hydrazide of valine.

As is well known, Wieland [4] has shown that thiophenyl esters may be decomposed by the action of enzymes. We investigated the possibility of decomposing the prepared thioesters by proteolytic enzymes: the thioester of phenylalanine by crystalline chymotrypsin, and of alanine by a commercial preparation of impure papain. It was shown that these substances were not decomposed by the enzymes mentioned; this was established by the absence of spots of phenylalanine and alanine on the chromatogram after incubation of the thioesters with enzymes and subsequent treatment of the mixture with hydrazine hydrate. In controlled experiments, analogous treatment of samples containing phthaloylamino acids produced clear spots on the amino acids on the chromatograms.

EXPERIMENTAL

The phthaloylamino acids were prepared from the amino acids and phthalic anhydrides in the usual manner, the trichlorothiophenol employed was recrystallized twice from benzene, m.p. 109.5—110.5°.

2,4,5-Trichlorothiophenol ester of N-phthaloyl-DL-alanine (VIII). Into a flask fitted with a reflux condenser was placed 0.7 g (0.03 mole) of (III) and 0.28 g $SOCl_2$ in 10 ml dry benzene, the mixture was heated until the solid completely dissolved, the solvent was evaporated off in vacuo at 30°, the residue dissolved in 5 ml of benzene, and treated with 0.82 g (I) (0.03 mole) in 10 ml of benzene and 0.5 ml of pyridine, then heated for 5 hours at 30°. The precipitated pyridine hydrochloride was filtered off and the filtrate evaporated in vacuo, 1 ml of ethyl acetate was added, and the mixture evaporated to dryness again. The solid residue was recrystallized from ethyl acetate to give 0.84 g (62.7%) (VIII) m.p. 135-137.5°. After recrystallization a further 0.16 g of material was isolated from the mother liquor; total yield 74.8%.

Found %: C 48.98, 49.15; H 2.71, 2.31; N 3.09, 3.09; Cl 25.62. $C_{17}H_{10}O_3NSCl_3$. Calculated %: C 49.23; H 2.43; N 3.37; Cl 25.69.

2,4,5-Trichlorothiophenyl ester of N-phthaloyl-DL-phenylalanine (IX). A mixture of the acid chloride (VI) (prepared as described above), and (I), on standing for 20 hours at 20° in the presence of pyridine, produced 72.3% (IX); after recrystallization from ethyl acetate (IX) had m.p. 186—187° (microdetermination).

Found %: C 56.10, 56.03; H 3.04, 3.00; N 2.57; Cl 21.79, 21.76. $C_{23}H_{14}O_3NSCl_3$. Calculated %: C 52.26; H 2.80; N 2.85; Cl 21.69.

2,4,5-Trichlorothiophenyl ester of N-phthaloyl-DL-valine (VII). In an analogous manner, from 0.5 g (IV), 0.15 ml (II), and 0.52 g (I) there was produced 0.55 g (61.5%) (VII) m.p. 132—133° (microdetermination).

Found %: C 51.43, 51.42; H 3.24, 3.17. $C_{19}H_{14}O_3NSCl_3$. Calculated %: C 51.53; H 3.19.

2,4,5-Trichlorothiophenyl ester of N-phthaloyl-DL-leucine (X). In an analogous manner, from 0.5 g (V) there was produced 0.48 g (55.3%) (X) in the form of an oil which crystallized on prolonged standing in vacuo over P_2O_5, m.p. 34—35° (recrystallized from a mixture of ethyl acetate and petroleum ether).

Found %: C 52.41, 52.43; H 3.87, 3.70; N 2.80, 2.91. $C_{20}H_{16}O_3NSCl_3$. Calculated %: C 52.54; H 3.54; N 3.06.

The action of hydrazine hydrate on the trichlorothiophenyl ester of phthaloylvaline (VII). To 0.1 g (VII) in 5 ml of absolute alcohol was added 1 ml of 67% hydrazine hydrate; the solid dissolved completely to give a yellow solution. After 2—3 hours a voluminous precipitate (I) had collected which was filtered off; the filtrate was evaporated to dryness in vacuo and treated with a 2% solution of HCl. The precipitate of phthaloyl hydrazide was filtered off and the solution again concentrated in vacuo. The residue was dissolved in 0.5 ml of water and 30 μliter of this solution applied to a chromatogram ("Leningrad No. 1" paper; solvent, pyridine—butanol—acetic acid—water 20 : 30 : 6 : 24). After developing with a 0.2% solution of ninhydrin, except for the yellow spot of hydrazine, with R_f 0.39, there was found only one other spot on the chromatogram with R_f 0.74 belonging to the hydrazide of DL-valine.

Treatment of trichlorothiophenyl esters of phthaloylphenylalanine and phthaloylalanine with enzymes.* A mixture of 2 mg of (IX) and 0.3—0.4 ml of a solution containing 2 mg of crystalline chymotrypsin in 1/15 mole phosphate buffer at pH 7.8, was shaken for 3 hours at 37°C. In controlled experiments, (VI) was treated with chymotrypsin, and (IX) and (VI) were incubated without enzymes. Afterward, each sample was treated with 0.5 ml of 67% hydrazine hydrate and heated for a further 30 minutes at 37°, then examined chromatographically. After developing, no phenylalanine was found in the test standards, but in the controlled tests with (VI), a clear spot of the amino acid developed.

Analogous results were obtained by treatment of (VIII) with papain, previously activated by hydrogen sulfide[5].

SUMMARY

1. Trichlorothiophenyl esters of phthaloylamino acids were synthesized in 61—75% yield.

2. The thioesters prepared do not react with esters of aminoacids and are stable towards the action of protolytic enzymes.

*This part of the work was carried out by L. I. Ivanov.

LITERATURE CITED

[1] T. Wieland, W. Schäfer and E. Bokelmann, Lieb. Ann. 573, 99 (1951).

[2] T. Wieland and H. Bernhard, Lieb. Ann 582, 218 (1953).

[3] J. A. Farrington, P. J. Hextall, G. W. Kenner and J. M. Turner, J. Chem. Soc. 1407 (1957).

[4] T. Wieland and H. Köppe, Lieb. Ann. 588, 15 (1954).

[5] J. L. Abernethy and I. Nakamura, J. Org. Ch. 23, 586 (1958).

SYNTHESIS OF CYCLIC AND LINEAR ORGANOSILOXANES WITH MIXED ALIPHATIC RADICALS AT THE SILICON ATOM

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Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4059–4063, December 1959

Original article submitted October 17, 1958

The aqueous hydrolysis of organochlorosilanes in the presence of a solvent produces polyorganosiloxanes of both cyclic and linear structure.*

In this work a study of the hydrolysis reaction of alkylhalogenosilanes with mixed radicals at the silicon atom was undertaken with the object of producing cyclic organosiloxanes, and also the cohydrolysis reaction of organochlorosilanes with mixed radicals at the silicon atom with trimethylchlorosilane to produce linear organosiloxanes.

For the production of cyclic organosiloxanes, the hydrolysis of the organochlorosilanes was conducted in strongly acidic aqueous medium without a solvent, or in the presence of ether. The strongly acidic conditions promote the reaction leading mainly to formation of cyclic organosiloxanes.

The hydrolysis of methylethyldichlorosilane, methylbutyldichlorosilane, and methylhexyldichlorosilane proceed by the following scheme:

$$n\,\begin{matrix}CH_3\\R\end{matrix}\!\!>\!SiCl_2 + 2H_2O \longrightarrow \left[\begin{matrix}CH_3\\R\end{matrix}\!\!>\!SiO\right]_n + 2nHCl,$$

$n = 3, 4, 5, 6$; $R = C_2H_5$, C_4H_9, C_6H_{13}.

Cyclic compounds containing different radicals at the silicon atom and having rings of from six to twelve members, were isolated from the hydrolysis of methylethyldichlorosilane, methylbutyldichlorosilane, and methylhexyldichlorosilane. The properties of the new compounds are given in Table 1.

Linear organosiloxanes with mixed organic radicals at the silicon atom, and trimethyl chain-terminating groups, were produced by the cohydrolysis of methylethyldichlorosilane, methylbutyldichlorosilane, methylhexyldichlorosilane, and isohexylmethyldichlorosilane with trimethylchlorosilane. The reaction was conducted in an acidic medium. The reactions were carried out at 90° to ensure fast reaction between the reacting components. The experiments showed that the reaction occurred by the scheme:

$$\begin{matrix}R\\CH_3\end{matrix}\!\!>\!SiCl_2 + 2(CH_3)_3SiCl \xrightarrow{H_2O} (CH_3)_3Si{-}O{-}\underset{\displaystyle CH_3}{\overset{\displaystyle R}{\underset{|}{\overset{|}{Si}}}}{-}OSi(CH_3)_3 + 3HCl$$

It should be noted that in spite of the high cohydrolysis temperature and the considerable excess of trimethylchlorosilane—the chain-terminating compound— some deviation from this mechanism was observed, with the side formation of cyclic compounds. Thus, for example, in addition to linear compounds, the cohydrolysis of methyl-

*Cf. J. Hyde and R. Delong, J. Am. Chem. Soc. 70, 1154 (1948).

TABLE 1

Compound	Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR found	MR calculated
1,2,3-Trimethyltriethylcyclotrisiloxane	$(CH_3C_2H_5SiO)_3$	197.5° (767)	1.4110	0.9360	70.15	69.93
1,2,3,4-Tetramethyltetraethylcyclotetrasiloxane	$(CH_3C_2H_5SiO)_4$	243.0 (767)	1.4164	0.9450	93.54	93.24
1,2,3,4,5-Pentamethylpentaethylcyclopentasiloxane	$(CH_3C_2H_5SiO)_5$	285.7 (767)	1.4208	0.9583	116.42	116.55
1,2,3,4,5,6-Hexamethylhexaethylcyclohexasiloxane	$(CH_3C_2H_5SiO)_6$	324.6 (767)	1.4245	0.9661	139.9	139.18
1,2,3-Trimethyltributylcyclotrisiloxane	$(CH_3C_4H_9SiO)_3$	260.0 (769.6)	1.4200	0.8865	97.14	97.71
1,2,3,4-Tetramethyltetrabutylcyclotetrasiloxane	$(CH_3C_4H_9SiO)_4$	291.0 (769.6)	1.4300	0.9230	130.20	130.28
1,2,3,4,5-Pentamethylpentabutylcyclopentasiloxane	$(CH_3C_4H_9SiO)_5$	312.0 (769.6)	1.4400	0.9464	161.80	162.85

TABLE 2

Compound	Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR found	MR calculated
Heptamethyl-3-ethyltrisiloxane	$(CH_3)_3SiOSiOSi(CH_3)_3$ (CH₃ on middle Si, C_2H_5 on middle Si)	171.7° (767)	1.3940	0.8204	72.95	72.55
Heptamethyl-3-butyltrisiloxane	$(CH_3)_3SiOSiOSi(CH_3)_3$ (CH₃ on middle Si, C_4H_9 on middle Si)	210 (752)	1.4020	0.8302	81.66	81.54
Heptamethyl-3-hexyltrisiloxane	$(CH_3)_3SiOSiOSi(CH_3)_3$ (CH₃ on middle Si, C_6H_{13} on middle Si)	230–241 (741.5)	1.4107	0.8442	90.12	90.39
Isohexylheptamethyltrisiloxane	$(CH_3)_3SiOSiOSi(CH_3)_3$ (CH₃ and C_6H_{13} on middle Si)	224–230 (737.5)	1.4150	0.8507	90.28	90.39

ethyldichlorosilane and trimethylchlorosilane produced 32.11% of cyclic compounds; the cohydrolysis of methylbutyldichlorosilane and trimethylchlorosilane, 21.46%; and the cohydrolysis of methylhexyldichlorosilane and trimethylchlorosilane, 20.58% of cyclic compounds. The properties of the linear siloxanes with mixed radicals at the silicon atom are given in Table 2.

EXPERIMENTAL

The following reactants were used: trimethylchlorosilane b.p. 57° (chlorine content 33.4%), methylethyldichlorosilane b.p. 100° (744 mm), methylhexyldichlorosilane b.p. 204° (745 mm), isohexylmethyldichlorosilane b.p. 204° (745 mm).

The synthesis of cyclic ethylmethylpolysiloxanes. Aqueous hydrolysis. Into a flask provided with a stirrer, reflux condenser, dropping funnel, and thermometer, was placed 250 ml distilled water. Then, with vigorous

stirring, 100 g of methylethyldichlorosilane was added to the water layer during 1.5 hours. The temperature of the reaction mixture was maintained at 20–22° during the addition process.

The oily layer of reaction product was separated from the water, and washed repeatedly with water until it gave a negative test for chloride ion. The washed reaction product was dried and fractionated. Yield of oil 49 g (79.6%). A fraction was isolated, 1,2,3,4-tetramethyltetraethyltetrasiloxane, produced in yield of 8.87 g (18.1% on fractionated mixture) with b.p. 236–242° (750.5 mm), d_4^{20} 0.9570, n_D^{20} 1.4169 MR_D 92.68, Calc. 93.24.

Found %: C 40.35; H 9.15; Si 30.97. M 343.3, 366, 394.2. $C_{12}H_{32}O_4Si_4$. Calculated %: C 40.86; H 9.14; Si 31.85. M 352.75.

Hydrolysis in the presence of a solvent. Into a three-necked flask provided with a stirrer, reflux condenser and thermometer, was placed 200 ml distilled water and 100 g diethyl ether. From a dropping funnel, 100 g methylethyldichlorosilane in 100 ml ether was added during 1.5 hours. The reaction was carried out at 0–2°. When reaction was complete, the ether layer was separated, washed, dried, and the solvent distilled off. An oil was obtained, 45 g (73.1%). The liquid was then distilled using a fractionating column (10 theoretical plates). The following compounds were obtained:

(1) 27.83 g (45.1% based on weight of distilled mixture) 1,2,3-trimethyltriethylcyclotrisiloxane. B.p. 197.5° (767 mm), d_4^{20} 0.9360, n_D^{20} 1.4110, MR 70.15; calc. 69.90.

Found %: C 40.81; H 9.23; Si 32.33. M 265. $C_9H_{24}O_3Si_3$. Calculated %: C 40.86; H 9.14; Si 31.85. M 264.6.

(2) 5.37 g (10.2% based on distilled mixture) 1,2,3,4-tetramethyltetraethylcyclotetrasiloxane with b.p. 243° (767 mm), d_4^{20} 0.9450, n_D^{20} 1.4164, MR 93.54; calc. 93.2.

Found %: C 40.93; H 9.32; Si 31.42. M 353.0. $C_{12}H_{32}O_4Si_4$. Calculated %: C40.86; H 9.14; Si 31.85. M 352.7.

(3) 0.423 g (0.69% based on distilled mixture) 1,2,3,4,5-pentamethylpentaethylcyclopentasiloxane with b.p. 285.7° (767 mm), d_4^{20} 0.9583, n_D^{20} 1.4208, MR 116.4; calc. 116.55.

Found %: C 41.06; H 9.27; Si 32.33; M 400. $C_{15}H_{40}O_5Si_5$. Calculated %: C 40.86; H 9.14; Si 31.85; M 440.9.

(4) 0.192 g (0.31% based on distilled mixture) 1,2,3,4,5, 6-hexamethylhexaethylcyclohexasiloxane with b.p. 324.6° (767 mm), d_4^{20} 0.9661, n_D^{20} 1.4245, MR 139.9; calc. 139.2.

Found %: Si 32.38 M 500. $C_{18}H_{48}O_6Si_6$. Calculated %: Si 31.85. M 529.1.

The synthesis of cyclic methylbutylpolysiloxanes. Aqueous hydrolysis. The hydrolysis was carried out in a an analogous manner to the hydrolysis of methylethyldichlorosilane. In the hydrolysis, 100 g methylbutyldichlorosilane was used. There was obtained 68.5 g (59%) of oil. A fraction was isolated consisting of 1,2,3,4-tetramethyltetrabutylcyclotetrasiloxane, 5.42 g (7.91% based on distilled mixture), b.p. 290–303° (750.5 mm), d_4^{20} 0.9230, n_D^{20} 1.4300, MR 130.2; calc. 130.3.

Found %: C 51.45; H 10.07; Si 23.77. M 476. $C_{20}H_{48}O_4Si_4$. Calculated %: C 51.65; H 10.40; Si 24.17. M 465.

1,2,3,4,5-Pentamethylpentabutylcyclopentasiloxane was produced in yield of 2.55 g (3.72% based on distilled mixture), b.p. 301–307° (750.5 mm), d_4^{20} 0.9464, n_D^{20} 1.4400, MR 161.8; calc. 162.8.

Found %: C 50.99; H 10.18; Si 24.29. M 555.6. $C_{25}H_{60}O_5Si_5$. Calculated %: C 51.65; H 10.40; Si 24.17. M 581.2.

Hydrolysis in the presence of a solvent. The hydrolysis was carried out in an analogous manner to the hydrolysis of methylethyldichlorosilane in the presence of a solvent. 50 g methylbutyldichlorosilane in 50 ml ether was used. There was produced 17.5 g of oil (51.5%).

A fraction consisting of 1,2,3-trimethyltributylcyclotrisiloxane, 0.74 g (4.2% based on weight of oil) was produced, b.p. 260° (769.6 mm), d_4^{20} 0.9065, n_D^{20} 1.4200, MR 99.8; calc. 100.1.

Found %: C 49.60; H 10.37; Si 25.04. M 355.1. $C_{15}H_{36}O_5Si_5$. Calculated %: C 51.65; H 10.40; Si 24.17. M 348.7.

A fraction consisting of 1,2,3,4-tetramethyltetrabutylcyclotetrasiloxane, had b.p. 291° (769.6 mm). Yield 0.955 g (4.5% based on weight of oil), d_4^{20} 0.9230, n_D^{20} 1.4300, MR 130.2; calc. 130.3.

Found %: C 51.06; H 10.59; Si 24.03. M 425. $C_{20}H_{48}O_4Si_4$. Calculated %: C 51.05; H 10.40; Si 24.17. M 465.

A fraction consisting of 1,2,3,4,5-pentamethylpentabutylcyclopentasiloxane had b.p. 320° (769.6 mm). Yield 1.31 g (7.5% based on weight of oil), d_4^{20} 0.9464, n_D^{20} 1.4400, MR 161.8; calc. 162.8.

Found %: C 51.06; H 10.59; Si 24.03. M 555. $C_{25}H_{60}O_5Si_5$. Calculated %: C 51.65; H 10.40; Si 24.17. M 581.2.

The cohydrolysis of methylethyldichlorosilane with trimethylchlorosilane. Into a three-necked flask fitted with a stirrer, reflux condenser and thermometer, there was placed 300 ml distilled water. The water was heated to 90°. A mixture of 30 g methylethyldichlorosilane and 68.3 g trimethylchlorosilane was prepared. The mixture of chlorides was added to the water during 2 hours, while stirring vigorously. The reaction temperature was maintained at 90—92°. When all the methylethyldichlorosilane and trimethylchlorosilane mixture had been added, the oily layer of reaction product was separated from the aqueous layer and washed repeatedly with water until it gave a negative test for chloride ion. The washed reaction product was dried and distilled using a fractionating column (10 theoretical plates). Yield of oil, 33.91 g (64.46%).

A fraction was isolated consisting of heptamethyl-3-ethyltrisiloxane, with b.p. 171.5° (767 mm), yield 7.29 g (13.8%), d_4^{20} 0.8204, n_D^{20} 1.3940, MR 72.95; calc. 72.55.

Found %: C 43.00; H 10.53; Si 32.40. M 254.7. $C_9H_{26}O_2Si_3$. Calculated %: C 43.14; H 10.46; Si 33.63. M 250.6.

The cohydrolysis of methylbutyldichlorosilane with trimethylchlorosilane. The synthesis of heptamethyl-3-butyltrisiloxane was carried out in analogous manner. From 40 g methylbutyldichlorosilane and 75 g trimethylchlorosilane there was obtained 45 g oil (68.95%). On distillation, using a fractionating column (10 theoretical plates) there was isolated a fraction with b.p. 210° (752 mm), d_4^{20} 0.8302, n_D^{20} 1.4020, MR 81.7; calc. 81.5.

Found %: C 47.04; H 10.80; Si 30.10. M 274. $C_{11}H_{30}O_2Si_3$. Calculated %: C 47.31; H 10.75; Si 30.11. M 278.6.

The cohydrolysis of methylhexyldichlorosilane with trimethylchlorosilane. The synthesis of heptamethyl-3-hexyltrisiloxane was carried out in an analogous manner. From 40 g methylhexyldichlorosilane and 65.4 g trimethylchlorosilane there was obtained 35.7 g oil (58%). On distilling the oil, a fraction was isolated with b.p. 230—241° (741.5 mm), yield 11.18 g (18.27%), d_4^{20} 0.8445, n_D^{20} 1.4107, MR 90.1; calc. 90.4.

Found %: C 50.76; H 11.27; Si 26.94. M 282.0. $C_{13}H_{34}O_2Si_3$. Calculated %: C 50.91; H 11.17; Si 27.47. M 306.7.

The cohydrolysis of isohexylmethyldichlorosilane with trimethylchlorosilane. The synthesis of isohexylheptamethyltrisiloxane was carried out in an analogous manner. From 10 g isohexylmethyldichlorosilane and 16.3 g trimethylchlorosilane there obtained 8.07 g oil (52.7%). On distilling the oil, a fraction was isolated with b.p. 224—230° (737.5 mm), yield 2.99 g (19.5%), d_4^{20} 0.8507, n_D^{20} 1.4150, MR 90.3; calc. 90.4.

Found %: C 50.99; H 11.69; Si 26.23. M 317.9. $C_{13}H_{34}O_2Si_3$. Calculated %: C 50.91; H 11.17; Si 27.47. M 306.7

SUMMARY

1. The hydrolysis reaction of alkylchlorosilanes in aqueous medium was investigated. The following new cyclic compounds were prepared: 1,2,3-trimethyltriethylcyclotrisiloxane, 1,2,3,4-tetramethyltetraethylcyclotetrasiloxane, 1,2,3,4,5-pentamethylpentaethylcyclopentasiloxane, 1,2,3,4,5,6-hexamethylhexaethylcyclohexasiloxane, 1,2,3-trimethyltributylcyclotrisiloxane, 1,2,3,4-tetramethyltetrabutylcyclotetrasiloxane, 1,2,3,4,5-pentamethylpentabutylcyclopentasiloxane.

2. The cohydrolysis reaction of organochlorosilanes with mixed radicals at the silicon atom with trimethylchlorosilane was studied, and the new linear compounds heptamethyl-3-ethyltrisiloxane, heptamethyl-3-hexyltrisiloxane and isohexylheptamethyltrisiloxane were synthesized.

THE PREPARATION OF ALKYLPHENOLS FROM BORIC ESTERS OF PHENOL AND ALCOHOLS

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Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4063-4069, December 1959

Original article submitted December 25, 1958

Alkylborates in the presence of aluminum chloride may be used for alkylating aromatic hydrocarbons and phenol [1,2]. In the present work we report a more convenient method for synthesizing alkylphenols from boric esters. Alkyl phenyl borates undergo a rearrangement on heating in the presence of a catalytic amount of sulfuric acid, in which the alkyl group is transferred to the benzene nucleus. Hydrolysis of the boric esters formed produces alkylphenols.

The reaction was carried out in the following manner. The mixed alkylphenylborate was synthesized by esterifying boric acid by a mixture of the alcohol and phenol, for example:

$$2C_4H_9OH + C_6H_5OH + H_3BO_3 \longrightarrow (C_4H_9O)_2C_6H_5OB + 3H_2O, \quad (1)$$

$$C_4H_9OH + 2C_6H_5OH + H_3BO_3 \longrightarrow C_4H_9O(C_6H_5O)_2B + 3H_2O. \quad (2)$$

The synthesis was carried out by boiling the mixture in a Dean and Stark apparatus, removing the water formed in the reaction by the described method [3]. At the completion of the reaction, when distillation of the water ceased, a small amount of sulfuric acid was added to the mixture, and heating continued in the same apparatus. Further evolution of water then occurred, by the alkylation reaction:

$$(C_4H_9O)_2C_6H_5OB \xrightarrow{H_2SO_4} (C_4H_9C_6H_4O)BO + C_4H_8 + H_2O, \quad (3)$$

$$2C_4H_9O(C_6H_5O)_2B \xrightarrow{H_2SO_4} [C_4H_9C_6H_4O(C_6H_5O)B]_2O + H_2O. \quad (4)$$

On hydrolysis, the alkylphenols were produced. The reaction was selected to investigate boric esters of phenol and primary isobutanol, which isomerizes during the alkylation process, producing p-tert-butylphenol.

No o-tert-butylphenol was produced in our reactions, as occurred in other syntheses employing acid catalysts and relatively high temperatures [4]. Possibly substitution does not occur in the ortho position on account of steric hinderance. Dibutylphenols also are not formed. The alkene formed according to equation [3] was trapped by absorption in bromine water, and converted to the corresponding dibromide.

The boric esters decompose on heating in the presence of a small amount of sulfuric acid, forming the corresponding alkene and alcohol, for example:

$$2(C_4H_9O)_3B \longrightarrow 3C_4H_8 + 3C_4H_9OH + B_2O_3. \quad (5)$$

The reaction was investigated for triisobutyl, tripropyl, and tributyl borates. The reactions proceeded easily in the presence of small amounts of sulfuric acid, phosphoric anhydride, alumina, etc.

It might be supposed that in the alkylation of arylborates, decomposition occurs, and the alkene formed alkylates the boric ester. However, by passing isobutylene or ethylene through triphenyl borate under the same reaction conditions and in the presence of the same amount of sulfuric acid, practically no alkylphenols are formed. By increasing the acidity, the reaction with isobutylene gives a very small yield of alkylphenols.

If, instead of using the mixed ester, an equivalent mixture of 2 moles triisobutyl borate and 1 mole triphenyl borate is used, then with the same quantity of sulfuric acid, no reaction at all occurs. By increasing threefold the amount of sulfuric acid, alkylation proceeds, but the alkylphenols are formed in much poorer yield than from the mixed ester. Attempts to alkylate aromatic hydrocarbons (p-xylol and naphthalene) by triisobutyl borate under the same conditions gave negative results. Thus it is impossible to interpret the synthesis as the simple alkylation of triphenyl borate by triisobutyl borate. Finally it is possible that the alkylating agent is isobutanol. However, if sulfuric acid is added at the start of the synthesis to a mixture of isobutanol, phenol, and boric acid, alkylation proceeds with a poor yield. If the isobutanol is added drop by drop during the course of the reaction, the yield is even poorer.

It is most probable that the alkylphenols are produced from mixed esters of boric acid. Possibly intermolecular rearrangement occurs, as summarized by equation (3) and (4). Obviously these equations represent the over-all result of a complex process consisting of several successive reactions. It may be envisaged as a much more complex reaction in which esters of metaboric or polyboric acids participate. Polyboric acids are known to be strong enough to catalyze the esterification of carboxylic acids [3]. On this basis we attempted to carry out the alkylation by esters of metaboric acid in the absence of sulfuric acid. However, even under severe conditions (about 300°), alkylation did not proceed using isobutyl metaborate and cyclohexyl metaborate; after hydrolyzing the mixture, only the starting phenol was recovered. Synthesis of tert-butylphenol by metaborate alkylation in the presence of sulfuric acid gave a poorer yield than that obtained from diisobutyl(phenyl)borate. In that way excess boric acid is not necessary. In corresponding alkylation experiments with cyclohexyl metaborate, cyclohexene was formed; cyclohexylphenol was not formed at all.

According to O'Conner and Nace [5] it appears that the decomposition of metaborates on heating produces alkenes (or the corresponding cyclenes). In the presence of sulfuric acid, phenyl dicyclohexyl borate forms p-cyclohexylphenol. Simultaneously, a large amount of cyclohexene is formed, with a corresponding reduction in the yield of cyclohexylphenol. Thus metaborates do not alkylate arylborates. In addition, these experiments once more confirm that the described synthesis of alkylphenols does not occur by intermediate alkene (or corresponding cyclene) formation; on the contrary, such a side reaction hinders the formation of alkylphenols.

It should be noted that mixed boric esters (as is the case for many other mixed esters of inorganic acids) cannot be successfully obtained in the pure state, since on distillation, even in vacuum, they disproportionate to the corresponding symmetrical esters.

By the esterification of boric acid with a mixture of phenol and isobutanol, we produced a product boiling over a wide temperature range, i.e., a mixture of symmetrical and mixed esters. If the symmetrical trialkyl and triaryl borates are separated by distillation, and the middle fraction redistilled, then in practice, after 3-4 such fractionations, triisobutyl borate and triphenyl borate are produced in the pure state; the mixed ester (the intermediate fraction) disappears, i.e., disproportionation occurs during the distillation.

Previous studies, in particular the work of Thomas [6], gave similar results. Colclough, Gerrard and Lappert [7], who reaction phenoxyborondichloride with isobutanol, produced generally not the mixed ester, but only a mixture of triisobutyl and triphenyl borate.

In our own alkylation experiments, we undoubtedly had present an equilibrium mixture of borates. The best yield of p-tert-butylphenol was produced from diphenyl isobutyl borate [according to equation (3)]. However the disproportionation of diisobutyl phenyl borate produces a small amount of phenol as impurity, but the alkylation product (tert-butylphenol) is easily separated.

It is possible to assume that, having the equilibrium mixture,

$$(C_4H_9O)_2C_6H_5OB \rightleftarrows C_4H_9O(C_6H_5O)_2B + (C_4H_9O)_3B \rightleftarrows (C_4H_9O)_3B + (C_6H_5O)_3B$$

Preparation of Alkylphenols by the Rearrangement of Dialkyl (Phenyl) Borates

Alcohol		Alkylation conditions		Unchanged phenol (moles)	Alkylphenol					Dibromoalkane (or alkene)	Auxiliary liquid (for azeotropic distillation of water formed during esterification) and additional reaction conditions
name	moles	time (hours)	temperature		name	weight (in g)	yield (% based on phenyl) reacted	yield (% based on phenyl) charged	characterization		
Isobutyl	1	16	160-260°	0.10	p-tert-butylphenol	45.0	75	60	M.p. 97.5°, benzoate m.p. 81° (according to [9,10] 97.5°, 81-82°)	Dibromoisobutane, b.p. 148-152° n_D^{10} 1.5112 (according to [11] 149-151° 1.51186)	15 g isobutyl alcohol
Isobutyl	0.5	16	208-215	0.25	p-tert-butylphenol	20.3	54.2	27.1	The same	The same	0.5 mole alcohol added at once, and 0.5 mole drop by drop for 5 hours (during the course of the reaction)
Isobutyl	1	6	187-253	0.25	p-tert-butylphenol	24.1	64.2	32.1	The same	The same	The same
Butyl	1	15	205-245	0.24	Mixture of butylphenols	23.8	61	31.7	B.p. 100-158° (50 mm) [4]	1,2,-Dibromobutane, b.p. 165-169° d_0^{20} 1.8221 (according to [12]: 166°, 1.8204)	15 g butyl alcohol
Propyl	0.5	26	200-248	0.20	o- and p-isopropylphenols	24.5	60	36	B.p. 125-150° at 20 mm*; o-isopropylphenoxyacetic acid, m.p. 129-130° (according to [4,13] 130-131°)	1,2,-Dibromopropane, b.p. 140-143°, d_4^{20} 1.9398 (according to [14]: 141.69°, 1.9333)	Esterified at 90-142° with 20 ml benzene
Propyl	1	35	235-260	0.17	o- and p- isopropylphenols	14.0	31.2	20.6	p-isopropylphenoxy acetic acid, m.p. 80-81° (according to [4,13] 80.5-81°)	The same	The same
Cyclohexanol	1	8	149-185	0.20	p-cyclohexyl-	11.0	21.0	12.5	M.p. 127.5°, benzoate, m.p. 115-115.5° (according to [15] 128°, 114-114.5°)	Cyclohexene 49.0 g (60.0%), b.p. 80-82.5°, n_D^{20} 1.4466 (according to [16] 80-82°, 1.4469)	30 ml xylene. Sulfuric acid (0.1 ml)

* Derivative prepared from pure product after twice distilling in a 25 cm Widmer column

introduction of diisobutyl phenyl borate displaces the equilibrium in favor of its formation; this explains the comparatively high yield.

It is impossible, however, to assume that simultaneously with the alkylation there occurs a side reaction involving decomposition of triisobutyl borate present in the reaction mixture to form the alcohol and alkene. As was mentioned above, under these conditions such decomposition does not occur.

Reaction (4) probably proceeds in two stages:

$$C_4H_9O(C_6H_5O)_2B \longrightarrow C_4H_9C_6H_4O(C_6H_5O)BOH, \quad (6)$$

$$2C_4H_9C_6H_4O(C_6H_5O)BOH \longrightarrow [C_4H_9C_6H_4O(C_6H_5O)B]_2O + H_2O. \quad (7)$$

In addition to p-tert-butylphenol and p-cyclohexylphenol, o- and p-isopropylphenols were prepared in an analogous manner from phenyl propyl borate, and a mixture of butylphenols from di-n-butyl phenyl borate (see table).

Nonphenolic products, including esters of phenol and other simple esters are not produced at all. Control was carried out by dissolving in alkali, as by Cohen[8]. This was to be expected, as the hydroxyl group of phenol is esterified by boric acid. After hydrolysis, the boric acid may be recovered pratically complete.

EXPERIMENTAL

Esterification of Boric Acid by a Mixture of Phenol and Isobutanol. Synthesis of diisobutyl phenylborate. The synthesis was carried out in a Dean and Stark apparatus (a flask of 400-ml capacity fitted with a thermometer and reflux column, and closed with a calcium chloride tube). In the flask was placed 31 g boric acid, 47 g phenol, and 86 g isobutanol; 15 g of isobutanol was necessary to fill the water-separator tube in distilling off the water as an azeotropic mixture, i.e., it did not take part in the reaction. The mixture was refluxed on a sand bath until distillation of the water-isobutanol azeotrope ceased (26-27 ml distilled over during 10 hours). The temperature of the mixture was increased from 107 to 160°. The product (a viscous liquid) was used without further purification.

The preparation of p-tert-butylphenol. To the prepared cool mixture of boric esters, 0.5 ml of 92% sulfuric acid was added, and the mixture refluxed until distillation of water ceased (15 ml distilled off during 16 hours). The gasses passing through the condenser were absorbed in two Tishchenko bottles by bromine water (as the decolorized bromo adduct). The temperature was increased to 260°. At the end of the reaction, the mixture became dark, and solidified on cooling. Water (150 ml) was added, and the mixture heated for 1 hour on a boiling-water bath. It was then cooled and extracted with benzene for some time. The benzene extract was washed well with a solution of sodium chloride, then by a 3% solution of sodium bicarbonate, again by sodium chloride solution, and finally dried for 12 hours over magnesium sulfate. The benzene was distilled off and the residue fractioned under vacuum using a column of packed height 25 cm. There was obtained 9.5 g phenol (b.p. 85-110° at 20 mm) and 45 g p-tert-butylphenol (b.p. 85-90° at 5 mm); the latter crystallized on cooling. Yield 75% (on reacted phenol), 60% (on starting phenol). Residue in flask, 3 g.

After a second distillation or recrystallization from water, the p-tert-butylphenol had m.p. 97.5°. Benzoylation by benzoyl chloride produced the benzoate with m.p. 81° (recrystallized from alcohol) which agrees with literature values [9,10].

The contents of the two Tishchenko bottles were combined, the oily layer separated, washed well with 5% sodium hydroxide solution, and dried over magnesium sulfate. There was obtained 80 g dibromoisobutane. The product distilled at 148-152°; after two fractionations, it had n_D^{20} 1.5112 (Literature value [11]: b.p. 149-151°. n_D^{20} 1.51186).

Other alkylphenols were prepared in an analogous manner. The results are given in the table. The phenol and boric acid were used on 0.5 mole scale, with 0.5 ml 92% sulfuric acid. Esterification took about 10 hours. An excess of the reacting alcohol or a hydrocarbon was always added as an auxiliary liquid for azeotropically distilling off the water formed. Before alkylation, (i.e., before adding the sulfuric acid) the hydrocarbon was distilled off.

The synthesis of isobutyl diphenylborate. Phenol (94 g) and 37 g isobutanol were used with the addition of a further 15 g of alcohol for the water separator (altogether 52 g). The esterification was carried out as described above; 27 ml water distilled off, and the temperature of the mass at the end of the reaction was 204°.

Similarly, from this product, p-tert-butylphenol was obtained; 7 ml water distilled off at a temperature up to 260°. There was obtained 62.5 g phenol and 45 g p-tert-butylphenol (90% based on reacted phenol).

Alkylation of triphenyl borate by triisobutyl borate. In a 3-necked 100-ml flask fitted with thermometer and water separator, was placed 29 g triphenyl borate, 46 g triisobutyl borate and 0.3 ml 92% sulfuric acid. The mixture was heated on a sand bath (250-260°). No reaction occurred, and no water distilled over. After hydrolyzing and treating as described above, unreacted isobutanol and phenol were recovered. By increasing the amount of sulfuric acid to 1 ml, the reaction was found to proceed at 190-220°. During 7 hours 22.5 ml water and 15 ml isobutanol distilled off. Then the mixture was hydrolyzed and treated as described above. There was obtained 3 g unchanged phenol and 18.7 g (44.2%) p-tert-butylphenol, identified as explained in the table. In addition there was obtained 4.6 g of material with b.p. 242-260°, which was soluble in alkali (presumably polyalkylphenols).

Alkylation of triphenyl borate of isobutylene. In a 3-necked 100-ml conical flask fitted with a thermometer and reflux condenser was placed 29 g triphenyl borate and 1 ml 92% sulfuric acid. The flask was heated to 225-255°, and isobutylene, prepared by the decomposition of 46 g isobutyl borate with 2 ml sulfuric acid at 200-222° in a flask fitted with water separator, was passed through the mixture for 6 hours by means of a tube reaching to the bottom of the flask.

After passing the isobutylene, the product was cooled, hydrolyzed, and treated as usual. There was obtained unreacted phenol and a 5 g fraction with b.p. 210-220°. The product was soluble in alkali solution, but it was not possible to isolate any individual alkyl phenols.

Alkylation of triphenyl borate by ethylene. Dry ethylene (12 liters) was passed through triphenyl borate at 250° during 16 hours in the presence of sulfuric acid, under the conditions of the previous experiment. The reaction mixture was then treated as described above. There was obtained unreacted phenol and a 2 g fraction with b.p. 190-200°, from which it was impossible to isolate individual products. Increasing the reaction temperature to 270° did not improve the result.

Simultaneous esterification and alkylation by isobutanol. In a 100-ml 3-necked flask there was placed 29 g phenol, 45 g isobutyl alcohol, 6.2 g boric acid and 0.5 ml 92% sulfuric acid. The mixture was refluxed on a sand bath until the distillation of water ceased (8 hours), and then for a further 16 hours (24 hours altogether). The mixture was then hydrolyzed and treated as described above. In addition to isobutanol and phenol, there was obtained 5 g material with b.p. 190-230°. Pure tert-butylphenol was not isolated.

SUMMARY

The formation of alkylphenols from alkyl phenyl esters of boric acid was investigated. The reaction involves the rearrangement of mixed aliphatic-aromatic esters of boric acid.

LITERATURE CITED

[1] V.K. Kuskov and B.M. Sheiman, Doklady Akad. Nauk SSSR 106,479 (1956). *

[2] V.K. Kuskov, B.M. Sheiman, and Z.L. Maksimova, Zhur. Obshchei Khim. 27, 1454 (1957). *

[3] V.K. Kuskov and V.A. Zhukova, Izv. AN SSSR, Otdel. Khim. Nauk 733, (1956). *

[4] R. Stroh, R. Seydel, and W. Hahn, Angew. Chem. 69, 699 (1957).

[5] G.L. O'Connor and H.R. Nace, J. Am. Chem. Soc. 77, 1578 (1955).

[6] L.H. Thomas, J. Chem. Soc. 823 (1946).

[7] T. Colclough, W. Gerrard, and M.F. Lappert, J. Chem. Soc. 907 (1955).

[8] L.A. Cohen, J. Org. Chem. 22, 1333 (1957).

[9] R.A. Smith, J.Am. Chem. Soc. 55, 9718 (1933).

[10] S. Natelson, J. Am. Chem. Soc. 56, 1583 (1934).

* Original Russian pagination. See C. B. translation.

[11] W. Krestinsky, Ber. 55, 2757 (1922).

[12] M. Lepingle, Bull. Soc. Chim. 39, 741 (1926).

[13] C.F. Kolsh, J. Am. Chem. Soc. 53, 304 (1931).

[14] M.S. Kharash, J. Am. Chem. Soc. 57, 2469 (1935).

[15] B. Niederl and S. Natelson, J. Am. Chem. Soc. 53, 1928 (1931).

[16] S.S. Nametkin, Zhur. Russ. Khim. Obshch. 55, 59 (1922).

CYCLOSERINE AND RELATED COMPOUNDS

IX. SYNTHESIS OF SOME ISOXAZOLIDONES—5

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Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4069—4078, December 1959

Original article submitted December 10, 1958

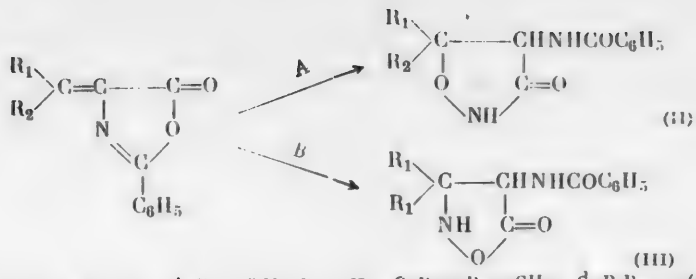
The great value of cycloserine as an efficient antituberculosis agent [1] has stimulated the appearance of a number of papers on the synthesis of analogs and derivatives of this antibiotic, for the purpose of studying the relation between biological activity and structure, and elucidating the mechanism of the action of isoxazolidones on micro- and macroorganisms.

Together with known routes of synthesizing cycloserine [2—5], a possible synthetic approach to isoxazolidones is cyclization of β-halo-substituted [6] and α, β-unsaturated hydroxamic acids. As we showed previously, α-benzoylamino-β-arylacrylhydroxamic acids, obtained by the reaction of 2-aryl-4-arylideneoxazolones-5 with hydroxylamine acetate [7], cyclized so readily to 2-aryl4-arylideneimidazolin-$\Delta^{1,2}$-ol-3-ones-4 [8], that it was impossible to obtain β-halohydroxamic acids required for the synthesis of isoxazolidones. It was also shown that cyclization of α-benzoylamino-β,β-dimethylacrylhydroxamic acid, obtained from 2-phenyl-4-isopropylideneoxazolone-5 by reaction with hydroxylamine, gave a substance which was similar in properties to 5-substituted isoxazolidone-3 [8]. As this reaction could provide a route for the synthesis of cycloserine analogs, we investigated it in more detail.

The reaction of 4-alkylideneoxazolidones-5 (I) with hydroxylamine was studied on the examples of 4-ethylidene- (Ia), 4-propylidene- (Ib), 4-isopropylidene- (Ic), and 4-cyclohexylideneoxazolidones-5 (Id). These compounds were obtained by known procedures, which, in the case of (Ia) and Ic), were substantially modified to make it possible to obtain higher yields and purer substances. A detailed study of the reaction of alkylideneazlactones with hydroxylamine acetate showed that if this reaction was carried out in the presence of a small amount of potassium acetate or with free hydroxylamine (pH ≥ 7), the substances formed were not hydroxamic acids (no reaction with ferric chloride) but corresponded in elementary analysis data to 5-alkyl-N-benzoylcycloserines and ultraviolet spectra analogous to that of 4-N-benzoylaminoisoxazolidone-3 (N-benzoylcycloserine).

However, these substances showed properties which would hardly be expected of 5-substituted N-benzoylisoxazolidones-3; the blue color with nitroprusside, characteristic of isoxazolidones-3 (Jones' reaction [9]), appeared only under certain conditions; the compounds were readily hydrolyzed by alkali, while isoxazolidones-3 are stable to alkaline hydrolysis [10]; these substances, like the hydrolysis products, reduced Fehling's solution in the cold, though O-alkylhydroxylamines are incapable of this reaction [11].

The data presented indicate that the direction of the reaction of alkylideneazlactones with hydroxylamine depends on pH and under the conditions we used in the present work (pH ≥ 7), led to the formation of heterocyclic compounds which could be either derivatives of isoxazolidone-3 (II) or derivatives of isoxazolidone-5 (III), i.e., the reaction proceeded either by route (A) or route (B).

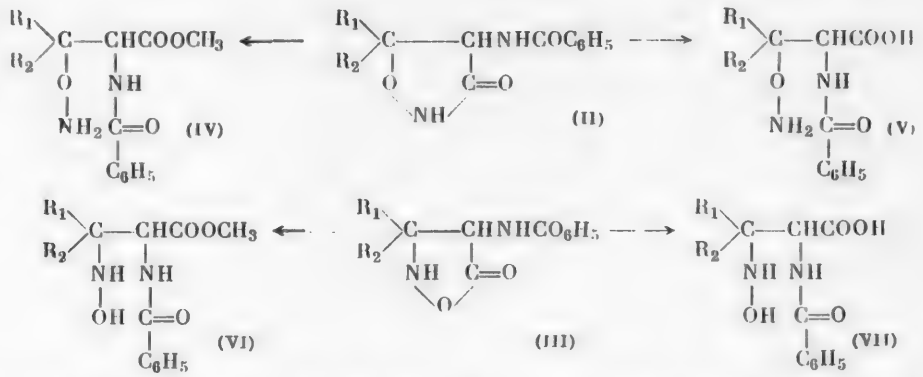


(II)

(III)

a $R_1 = CH_3$, $R_2 = H$; b $R_1 = C_2H_5$, $R_2 = H$; c $R_1 = R_2 = CH_3$; d $R_1R_2 = -(CH_2)_5-$.

In only one case, in the reaction of (Id) with hydroxylamine acetate, was it possible to isolate in low yield (~10%) a substance which gave a color with ferric chloride and was probably α-benzoylaminocyclohexylideneacetohydroxamic acid. Since the data presented above did not make it possible to make an unequivocal choice between structures (II) and (III), we studied the hydrolysis and reduction of the substances obtained in more detail. It was found that they were readily hydrolyzed in both acid and alkaline media to give high yields of the same substances, which corresponded in composition to the products of the addition of one molecule of water. Treatment with a methanol solution of hydrogen chloride formed the product from the addition of one mole of methanol (cf. [12]).



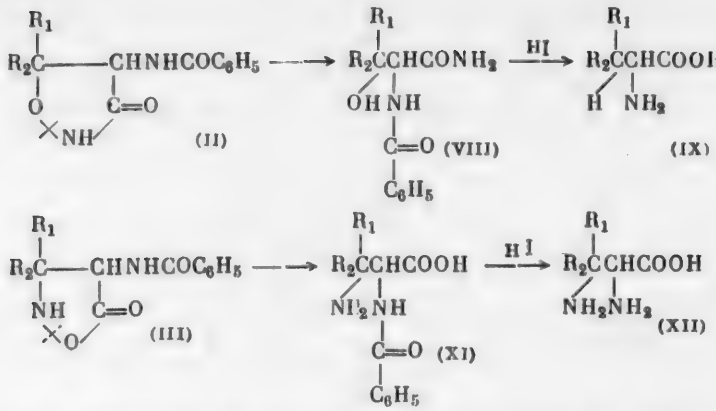
(IV) (II) (V)

(VI) (III) (VII)

The products of acidic methanolysis and hydrolysis of compounds (II) and (III) should be different, as in the first case, derivatives of α-benzoylamino-β-aminohydroxy-substituted acid (IV) and (V) should be formed and in the second, derivatives of α-benzoylamino-β-hydroxyamino-substituted acid (VI) and (VII). Since the hydrolysis products of compounds (Ic) and Id) and also the methanolysis product of (Ic) reduced Fehling's solution and did not show properties characteristic of O-hydroxylamine derivatives, the more acceptable structures are (VI) and (VII).

The infrared spectra of the methanolysis products showed a band at 3620 cm^{-1}, characteristic of an OH group, which can only be in the case of structure (VI), but not (IV). This conclusion was confirmed by catalytic hydrogenation of the hydrolysis products obtained. As is known [13], in this case O-derivatives of hydroxylamine undergo hydrogenolysis with the elimination of ammonia to form a hydroxy compound. On the other hand, N-derivatives of hydroxylamine should give amino derivatives on hydrogenation. It should be noted that the hydrogenation of N-substituted hydroxylamines proceeds with difficulty and only if the basic properties of the nitrogen atom are suppressed as in the case of compounds of type (III) (cf. [13]) ($K_B \leq 10^{-12}$, determined by titration in glacial acetic acid [14]) or with the use of a strongly protophilic solvent, as in the case of compounds in which the nitrogen atom shows basic properties [15, 16]. As a model experiment we hydrogenated β-hydroxyaminohydrocinnamic acid in aqueous ammonia and this gave a good yield of β-phenyl-β-alanine. By hydrogenation of the hydrolysis product of (Vc) or (VIIc) (in which the nitrogen atom in the hydroxyamino group had a basicity similar to that of the nitrogen in β-hydroxyaminohydrocinnamic acid) in triethylamine, we obtained a compound which corresponded in composition to the monobenzoyldiamino acid (XIc). This indicated that the hydrolysis product had structure (VII) and that the starting compound corresponded to structure (III).

Even more definite data supporting this conclusion were obtained by reduction of the reaction products of hydroxylamine and the azlactones. Reduction of compounds of structures (II) or (III) should occur with rupture of the O—N bond [10, 13] and the reduction products in the two cases should be the same.



On reduction with hydriodic acid, the primary reaction product (VIII), in addition to suffering hydrolysis of both amide groups, should be reduced to an α-amino acid, as is well known for hydroxyamino acids [17]. On the other hand, (XI) should given an α, β-diamino acid. Hydriodic acid reduction of the reaction products of hydroxylamine with (Ia) and (Ib) yielded α, β-diaminobutyric and α, β-diaminovaleric acids, respectively, which were identified as the dibenzoyl derivatives.

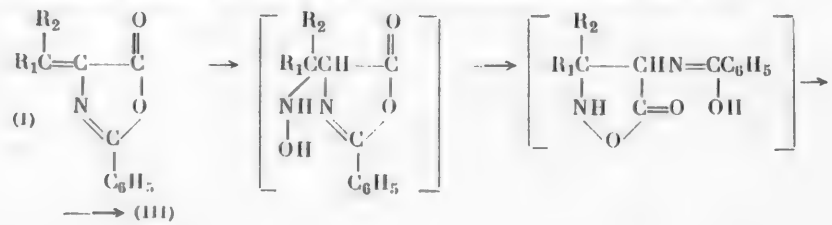
When hydrogenated over platinum oxide, the reaction products of azlactones and hydroxylamine gave compounds with one free nonamide amino group, as was demonstrated by titration in glacial acetic acid (cf. [18]), and consequently they had structure (XI). After hydrolysis and benzoylation, one of them(R_1= CH_3, R_2=H) gave α,β-dibenzoylaminobutyric acid, identical with the substance obtained by reduction of the corresponding isoxazolidone with hydriodic acid. Thus, data obtained by reduction and hydrolysis of the reaction products of alkylideneazlactones (I) and hydroxylamine show unequivocally that these products can only have structure (III) and are substituted isoxazolidones-5. Thus, the reaction of alkylideneazlactones with hydroxylamine proceeds differently to the reaction of their aromatic analogs [7], but likewise leads not to compounds of the cycloserine series, but their isomers.

It is interesting to note that the compounds we obtained are representatives of a previously unknown class of isoxazolidones-5 without substituents on the nitrogen atom. Compounds described by Shaw [19] as 3-alkyl-4-aminomethyleneisoxazolidones-5 do not correspond to this structure according to their properties and in all probability were ketimines of N-substituted α-aminomethyleneacetoacetic acids (cf. [20]).

In conclusion, it was necessary to establish the mechanism of the new reaction of 4-alkylidene-2-phenyloxazolones-5 with hydroxylamine, which, as was shown above, differs from the reaction of their aromatic analogs that give a high yield of α-benzoylamino- β-arylacrylhydroxamic acids under analogous conditions.

As is known, reactions of unsaturated azlactones may occur either at the semicyclic double bond or with ring opening and the direction of the reaction depends essentially on the nature of the substituents in the azlactone and the pH of the medium. In an acid medium the main direction of the reaction is opening of the azlactone ring [7,21], which is almost independent of the substituents. On the other hand, in an alkaline medium the direction of the reaction depends more on the nature of the substituents in position 4 and the reaction may proceed partially with addition at the double bond [22] when replacement of one or both substituents in the azlactone by aliphatic groups facilitates addition at the semicyclic double bond [23, 24].

On the basis of these data, one may represent the mechanism of the formation of 3-alkyl-4-benzoylaminoisoxazolidones-5, described above, in the following way: In the weakly alkaline or neutral media we used, a molecule of hydroxylamine adds at the semicyclic double bond and then the saturated azlactone formed internally acylates the hydroxyamino group with closure of the five-membered isoxazolidone ring.



This hypothesis is also confirmed by the fact that as is well-known [25], saturated azlactones, obtained by addition at the semicyclic double bond (which always occurs before opening of the azlactone ring), are very vigorous acylating agents.

EXPERIMENTAL

Synthesis of 2-Phenyl-4-Alkylideneoxazolones

2-Phenyl-4-ethylideneoxazolone-5 (Ia) was obtained by a modification of Peleger's procedure [26]. Hippuric acid (100 g) was ground with 35 g of anhydrous sodium acetate and stirred for 0.5 hour with 200 ml of acetic anhydride at 15–20°; then 120 ml of acetaldehyde was added over a period of 30–40 minutes at a temperature of no higher than 25°, and the mixture heated for 2 hours at 55–60°. On the following day, a further 70 ml of acetaldehyde was added and the mixture heated for a further 2.5–3 hours at the same temperature; the reaction mixture was poured onto ice and the precipitate collected, washed with water, and dried in air. The yield was 95–100 g (90–95%) and the m.p. 65–70°. The crude, dry oxazolone was dissolved in 100-150 ml of boiling alcohol and slowly cooled; the pure substance precipitated as fine, light-orange needles with m.p. 96–97°.

2-Phenyl-4-propylideneoxazolone-5 (Ib) was obtained by a known procedure [27] in 40–45% yield and had m.p. 80–82° (from alcohol).

2-Phenyl-4-isopropylideneoxazolone-5 (Ic). Hippuric acid (36 g) was ground with 12 g of anhydrous potassium acetate and 350 ml of acetone, and 25 ml of acetic anhydride added. The mixture was boiled for 30 minutes, the acetone removed in vacuum, and the residue poured onto ice. The precipitate [25–27 g (62–68%); m.p. 91–93°] was purified by recrystallization from 70% alcohol to yield 15–17 g (37–42%) of pure (Ic) with m.p. 97–98°; it formed thick orange prisms. The substance could also be purified by conversion into α-acylamino-β,β-dimethylacrylic acid and cyclization of the latter with acetic anhydride to (Ic).

Crude 2-phenyl-4-isopropylideneoxazolone-5 (25 g) was suspended in 1 liter of hot 2N hydrochloric acid, 50 ml of toluene added, and the mixture boiled with vigorous stirring for 30 minutes. The cooled mixture was filtered to yield 22.0–23.5 g (82–86%) of α-benzoylamino-β,β-dimethylacrylic acid with m.p. 216–218°.

Found %: N 6.56. $C_{12}H_{13}O_3N$. Calculated %: N 6.41.

α-Benzoylamino-β,β-dimethylacrylic acid (10 g) was boiled for 5 minutes with 40 ml of acetic anhydride, poured onto ice, and the precipitate collected and washed with water. The yield of (Ic) as almost colorless leaflets was 8.5–8.9 g (92–96%); the m.p. was 98–99°. Literature data [28]: m p. 94–97°.

2-Phenyl-4-cyclohexylideneoxazolone-5 (Id). This compound was obtained by a known procedure [29]; replacement of sodium acetate by potassium acetate made it possible to raise the yield to 65–70%; the m.p. was 137–138° (from a mixture of chloroform and alcohol).

Synthesis of 3-Alkyl- and 3,3-Dialkyl-4-Benzoylaminoisoxazolidones-5

3-Methyl-4-benzoylaminoisoxazolidone-5 (IIIa). To 10 g of (Ia) was added 200 ml of a 0.6 N methanol solution of hydroxylamine acetate (for the preparation of this solution, 105 ml of a 1.2 N methanol solution of potassium acetate was mixed with 95 ml of 1.2 N methanol solution of hydroxylamine hydrochloride, and the potassium chloride removed by filtration), after 6–12 hours the solution evaporated on a water bath in vacuum to 30–40 ml (temperature no higher than 30–35°), 15–20 ml of water added, and the mixture extracted with ethyl acetate. The extract was washed with water, dried with anhydrous sodium sulfate, evaporated to 20–30 ml in vacuum, 30–40 ml of dry dichloroethane added, and the mixture left overnight at -10°. The colorless precipitate was washed with dichloroethane and ether to yield 6.5–7.5 g (55–65%) of product; the m.p. was 179–181° (from water).

Found %: C 60.06; H 5.53; N 12.49. $C_{11}H_{12}O_3N_2$. Calculated %: C 59.95; H 5.44; N 12.69.

The substance was difficultly soluble in water, ether, and dichloroethane, but dissolved slowly in acids and alkalis with partial decomposition; it did not give a color with ferric chloride, but reduced Fehling's solution in the cold.

3-Ethyl-4-benzoylaminoisoxazolidone-5 (IIIb). This compound was obtained analogously from 10 g of (Ib) and 200 ml of 0.6 N hydroxylamine acetate solution and the yield was 5.6–6.2 g (50–55%); the m.p. was 156-157° (from aqueous alcohol).

Found %: C 61.40; H 6.11; N 11.78. $C_{12}H_{14}O_3N_2$. Calculated %: C 61.53; H 6.00; N 11.91.

3,3-Dimethyl-4-benzoylaminoisoxazolidone-5 (IIIc). To 10 g of (Ic) was added 200 ml of a 0.6 N methanol solution of hydroxylamine acetate, and after 4 hours the mixture was evaporated on a water bath in vacuum (temperature no higher than 30–35°) to a volume of 40–50 ml, 50 ml of water added, and the mixture extracted with ethyl acetate (4 × 50 ml). The ethyl acetate extract was washed with water, dried with sodium sulfate, and evaporated to 25–30 ml, and 50–70 ml of dry dichloroethane added. The colorless, crystalline precipitate was collected and washed with dichloroethane and ether. The yield was 8.5 g (73%) and the m.p. 149-152° (from alcohol, decomp.). It was possible to isolate a further 0.8–0.9 g of pure substance from the mother liquor. The total yield was 80–82%.

Found %: C 61.61; H 6.07; N 11.89. $C_{12}H_{14}O_3N_2$. Calculated %: C 61.53; H 7.00; N 11.91.

The same substance could be obtained in 40–60% yield by reaction of (Ic) with a methanol solution of hydroxylamine as the base. The substance was soluble in alcohol, ethyl acetate and acetone, and insoluble in water and ether; it reduced an alcohol solution of silver and Fehling's solution; it did not give a color with ferric chloride solution. Boiling with a methanol solution of ammonia did not change the substance. It gave a non-characteristic greenish blue color with nitroprusside.

3,3-Spiropentamethylene-4-benzoylaminoisoxazolidone-5 (IIId). To 10 g of (Id) was added 200 ml of a methanol solution of hydroxylamine acetate, and the mixture stirred until solution was complete (1.5–2 hours) and left overnight. The precipitate (4.5–5.5 g) was collected and washed with methanol. The mother solution was diluted with an equal volume of water to precipitate a further 3.8–5.0 g of a pinkish, crystalline powder. The latter was suspended in a 3–5% solution of sodium hydroxide, stirred vigorously for 5–10 minutes, and a further 2.5–3.0 g of substance collected by filtration. The total yield was 7–8.5 g (62–75%). Substance (IIId) was soluble in dioxane, but less so in methanol, and reduced Fehling's solution in the cold. After three recrystallizations from dioxane, the substance had m.p. 192–193°.

Found %: C 65.54; H 6.79; N 10.36. $C_{15}H_{18}O_3N_2$. Calculated %: C 65.67; H 6.62; N 10.20.

The alkaline solution after isolation of the second portion was acidified to precipitate a pinkish-white substance, which was apparently α-benzoylaminocyclohexylidenehydroxamic acid, and this was washed with water and ether; the yield was 1.0–2.0 g and the m.p. 134–135°; the substance was soluble in alkali and gave a violet color with ferric chloride.

Found %: C 66.06; H 6.79; N 10.24. $C_{15}H_{18}O_3N_2$. Calculated %: C 65.68; H 6.68; N 10.21.

Hydrolysis and Alcoholysis of Isoxazolidones-5

β-Hydroxyamino-β-methyl-α-benzoylaminobutyric acid (VIIc). a) Acid hydrolysis. (IIIc) (1 g) was dissolved in 100 ml of 15% hydrochloric acid. After 30 minutes the reaction mixture was carefully adjusted to pH 5.0–5.5 with sodium hydroxide solution. This precipitated 0.98 g (92%) of (VIIc) as a white, crystalline solid with m.p. 170–172°. b) Alkaline hydrolysis. (IIIc) (1 g) was dissolved in 35 ml of 1.5% sodium hydroxide solution and heated at 70–80° for 3–5 minutes; the reaction mixture was cooled and acidified to pH 5.0–5.5. This precipitated 0.95 g of (VIIc) with m.p. 169–172° (decomp.). The substance was difficultly soluble in water and organic solvents, but dissolved readily in acids and alkalis, including 5% sodium bicarbonate solution; it reduced Fehling's solution.

Found %: N 11.08. M 249.3. $C_{12}H_{16}O_4N_2$. Calculated %: N 11.09. M 251.3.

β-Hydroxyamino-β,β-cyclopentamethylene-α-benzoylaminopropionic acid (VIIId) [R_1, R_2 = $-(CH_2)_5$]. A suspension of 5 g of (IIId) in 100 ml of 5% sodium hydroxide was heated on a water bath (60–70°) until solution was complete (20–30 minutes). The solution was cooled and acidified to pH 6; the precipitate was collected and washed with water and ether. The yield of (VIIId) was 5.1 g (95%) and the m.p. 176–178° (from alcohol). The substance was soluble in alcohol, bicarbonate solutions, and acids (at pH ≤ 4.5), did not give a color with ferric chloride, but reduced Fehling's solution in the cold.

Found %: N 9.66. $C_{15}H_{20}O_4N_2$. Calculated %: N 9.58.

Methyl β-hydroxyamino-β-methyl-α-benzoylaminobutyrate hydrochloride (VIc). A solution of 4 g of (IIIc) in 40 ml of a 7% solution of hydrogen chloride in anhydrous methanol was left for 20 hours at room temperature, the methanol removed in vacuum, the residue dissolved in dry ethyl acetate, and chloroform and ligroin

added. The liberated oil rapidly crystallized completely. The yield of (VIc) was 3.9 g (75%) and the m.p. 138–141° (decomp.). A further 0.2–0.5 g of (VIc) could be isolated from the mother liquor. The substance was soluble in water, alcohols, and dichloroethane, reduced Fehling s solution in the cold, and was quantitatively converted into (VIIc) by treatment with aqueous alkali.

Found %: C 51.48; H 6.40, N 9.55; Cl 11.67. $C_{13}H_{19}O_4N_2Cl$. Calculated %: C 51.56; H 6.27; N 9.25; Cl 11.7.

β-Phenyl-β-alanine. To a solution of 3 g of β-hydroxyaminohydrocinnamic acid (for preparation see [30]) in 50 ml of methanol was added 15 ml of aqueous ammonia and the material hydrogenated over platinum oxide. After 6 hours the theoretical amount of hydrogen had been absorbed and the solution did not reduce Fehling's solution. After removal of the catalyst, the solution was evaporated to 20 ml and diluted with alcohol to precipitate 1.9 g of β-phenyl-β-alanine with m.p. 218–219° (from aqueous alcohol). Literature data: m.p. 221° [31].

β-Amino-β-methyl-α-benzoylaminobutyric acid. A sample of 3 g of (VIIc) was dissolved in 50 ml of dry triethylamine and hydrogenated over platinum oxide. The equivalent amount of hydrogen had been absorbed after 18 hours and the solution did not reduce Fehling's solution. Removal of the catalyst and evaporation yielded 2.6 g of (XIc) with m.p. 227–229°. A mixed melting point with the sample described below was not depressed.

Reduction of Isoxazolidones-5

1. Hydrogenolysis

β-Amino-α-benzoylaminobutyric acid (XIa). A sample of 2 g of (IIIa) in 50 ml of methanol was hydrogenated in the presence of 0.1 g of platinum oxide. The equivalent amount of hydrogen had been absorbed after 1 hour. After the addition of 5 ml of ml of aqueous ammonia, the catalyst was removed by filtration and the filtrate evaporated to 30–35 ml in vacuum. The white precipitate (0.85 g, 42%) was collected and washed with alcohol and ether; it had m.p. 229-231° (from aqueous alcohol). A further 0.6–0.8 g of product with m.p. 224–228° could be isolated from the mother liquor. The total yield was 70–80%.

The substance was readily soluble in water, less so in alcohol, did not give a color with ferric chloride, and did not react with Fehling's solution.

Found %: C 59.22; H 6.35; N 12.35. $C_{11}H_{14}O_3N_2$. Calculated %: C 59.46; H 6.35; N 12.61.

A sample of 0.5 g of (XIa) was boiled with 15 ml of concentrated hydrochloric acid for 2 hours, the benzoic acid extracted with ether, and water evaporated from the residue, which was then made alkaline and benzoylated with 2 ml of benzoyl chloride. After acidification of the mixture, the precipitate was washed with water and ether; the yield of α, β-dibenzoylaminobutyric acid was 0.41 g; the m.p. was 216-217°.

β-Amino-α-benzoylaminovaleric acid (XIb). This compound was obtained analogously by hydrogenation of (IIIb); the yield was 68–75% and the m.p. 190–192° (from aqueous alcohol).

Found %: C 60.61; H 6.96; N 12.18. M 237.1. $C_{12}H_{16}O_3N_2$. Calculated %: C 60.98; H 6.86; N 11.86. M 236.3.

β-Amino-β-methyl-α-benzoylaminobutyric acid (XIc). A sample of 5 g of (IIIc) was suspended in 100 ml of water and hydrogenated over 0.1 g of platinum oxide. The theoretical amount of hydrogen had been absorbed after 30–40 minutes. The catalyst was removed by filtration, the filtrate evaporated to 15–20 ml, and 30 ml of alcohol added. This precipitated 3.8 g (75%) of (XIc) with m.p. 227–229° (from alcohol). A further 0.8–0.9 g of the substance could be isolated from the mother liquor. The total yield was 89–93%. The substance was soluble in water, less so in alcohol, and insoluble in ether and acetone; it did not reduce Fehling's solution.

Found %: C 60.82; H 7.16; N 11.59. M 236.9. $C_{12}H_{16}O_3N_2$. Calculated %: C 60.98; H 6.86; N 11.86. M 236.3.

β-Amino-β-cyclopentamethylene-α-benzoylaminopropionic acid. A sample of 5.5 g of (IIId) was suspended in 100 ml of methanol, 0.1 g of platinum oxide added, and the mixture hydrogenated; the equivalent amount of

hydrogen was absorbed after 35—40 minutes, and during the hydrogenation the precipitate dissolved and again precipitated. A 10% solution of alkali was added to the suspension until solution was complete and then the catalyst was removed by filtration and the filtrate acidified to pH 6, to precipitate 5.3 g (97%) of a white, crystalline solid with m.p. 320—330° (decomp., from aqueous dioxane). The substance was soluble in alkalis, and in acids at pH < < 5.0; it did not give a color with ferric chloride or reduce Fehling's solution.

Found %: C 65.22; H 7.67. $C_{15}H_{20}O_3N_2$. Calculated %: C 65.20; H 7.30.

2. Reduction with Hydriodic Acid

α, β-Dibenzoylaminobutyric acid. A sample of 2 g of (IIIa) was dissolved in 20 ml of 50% hydriodic acid, 1 g of red phosphorus and 0.6 g of iodine added, and the mixture boiled for 6 hours on a mantle. At the end of the reaction, the excess phosphorus and the benzoic acid were removed by filtration and the filtrate diluted to 300 ml and evaporated to 50 ml; a further 150 ml of water was added and the solution again evaporated to 50 ml. The residue was made alkaline and benzoylated by the Schotten-Baumann method with 5 ml of benzoyl chloride and the pH kept at 8-9. After 2 hours the reaction mixture was acidified and the precipitate collected and washed with water and ether. Recrystallization from aqueous alcohol yielded a colorless substance with m.p. 225-227°.

Found %: C 66.45; H 5.81; N 8.63. $C_{18}H_{18}O_4N_2$. Calculated %: C 66.25; H 5.56; N 8.58.

α, β-Dibenzoylaminovaleric acid. This compound was obtained analogously by reduction of (IIIb) with 50% hydriodic acid; the yield was 50% and the m.p. 216—217° (from alcohol).

Found %: C 67.31; H 6.19. $C_{19}H_{20}O_4N_2$. Calculated %: C 67.08; H 5.92.

SUMMARY

1. A method was developed for synthesizing 3-alkyl-4-benzoylaminoisoxazolidones-5 by reaction of 2-phenyl-4-alkylideneoxazolones-5 with hydroxylamine in a weak alkaline or neutral medium, and ideas are put forward on the mechanism of this reaction.

2. The structure of the compounds obtained was demonstrated by hydrolysis in acid and alkaline media, leading to β-hydroxyamino-α-benzoylamino-substituted acids, and by hydrogenolysis, leading to β-amino-α-benzoylamino-substituted acids.

LITERATURE CITED

[1] N. K. Kochetkov, R. M. Khomutov and M. Ya. Karpeiskii, Antibiotics, No. 1 [in Russian] (IL, 1959), [69], p. 32.

[2] C. H. Stammer, A. N. Wilson, F. W. Holly and K. Folkers, J. Am. Chem. Soc. 77, 2346 (1955); C. H. Stammer, A. N. Wilson, C. Spenser, F. Bachelor, F. W. Holly and K. Folkers, J. Am. Chem. Soc. 79, 3236 (1957).

[3] N. K. Kochetkov, R. M. Khomutov and M. Ya. Karpeiskii, Doklady Akad. Nauk SSSR, 111, 831 (1956); • Zhur. Obshchei Khim. 28, 3013 (1958).•

[4] J. Smrt, I. Beranek, J. Sicher and P. Šorm, Chem. Listy, 51, 112 (1957).

[5] Pl. Plattner, A. Boller, H. Frick, A Fürst, B. Hegdüs, H. Kirschensteiner, St. Majnom and R. Spiegelberg, Helv. Chim. Acta, 40 1531 (1957).

[6] N. K. Kochetkov, R. M. Khomutov, E. S. Severin, M. Ya. Karpeiskii, É. I. Budovskii and V. I. Erashko, Zhur. Obshchei Khim. 29, 3417 (1959). •

[7] N. K. Kochetkov, É. I. Budovskii, R. M. Khomutov and M. Ya. Karpeiskii, Zhur. Obshchei Khim. 29, 69 (1959). •

[8] N. K. Kochetkov, É. I. Budovskii, R. M. Khomutov, and M. Ya. Karpeiskii, Zhur. Obshchei Khim., 29, 635 (1959).•

•Original Russian pagination. See C. B. translation.

[9] L. Jones, J. Anal. Chem. 28, 39 (1956).

[10] R. Ratouis and R. Bechar, C.r. 243, 966 (1957).

[11] A. Behrend, Lieb. Ann. 257, 206 (1891); H. A. Janny, Ber. 16, 175 (1893).

[12] R. Ratouis and R. Bechar C. r. 243, 966 (1957).

[13] R. M. Khomutov, M. Ya. Karpeiskii, E. I. Budovskii, E. S. Severin and N. K. Kochetkov, Zhur. Obschei Khim. 29 (642 (1959). •

[14] Sh. Pallit. Nonaqueous Titration [in Russian] (State Chem. Press, 1958).

[15] L. Neelakantan and W. Hartung, J. Org. Ch. 23, 967 (1958).

[16] K. Hoy and W. Hartung, J. Org. Ch. 23, 965 (1958).

[17] E. Fischer, Ber. 35, 3787 (1902); E. Abderhalden and K. Heyns, Ber 67, 531 (1934).

[18] G. Nadeau and L. Branchen, J. Am. Chem. Soc. 57, 1363 (1935).

[19] G. Shaw, J. Chem. Soc. 720 (1950); 1017 (1951); 3482 (1952).

[20] A. Panizzy, Gazz. 76, 44 (1946).

[21] The Chemistry of Penicillin, 790 (1949).

[22] E. Shaw and J. M. Dowell, J. Am. Chem. Soc. 71, 1691 (1949).

[23] H. Carter, Ph. Handler and D. Melville, J. Biol. Chem. 129, 359 (1939).

[24] The Chemistry of Penicillin, 785 (1949).

[25] Organic Reactions [Russian translation] (IL, 1951) Vol. III.

[26] R. Peleger and M. Strandtmann, Ber. 90, 460 (1957).

[27] The Chemistry of Penicillin,783 (1949).

[28] S. I. Lur'e, E. S. Chaman and G. A. Ravdel', Zhur. Obshchei Khim. 23, 1392 (1953). •

[29] G. Brown and S. Safir, J. Org. Ch. 12, 483 (1947).

[30] Th. Posner, Ber. 36, 4310 (1903).

[31] Synthesis of Organic Preparations [Russian translation] (1952), Vol. III, p. 262.

•Original Russian pagination. See C. B. translation.

SOME DERIVATIVES OF α,β-DIPHENYLETHYLENEDIAMINE

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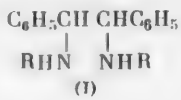
Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4078–4081, December, 1959

Original article submitted December 10, 1958

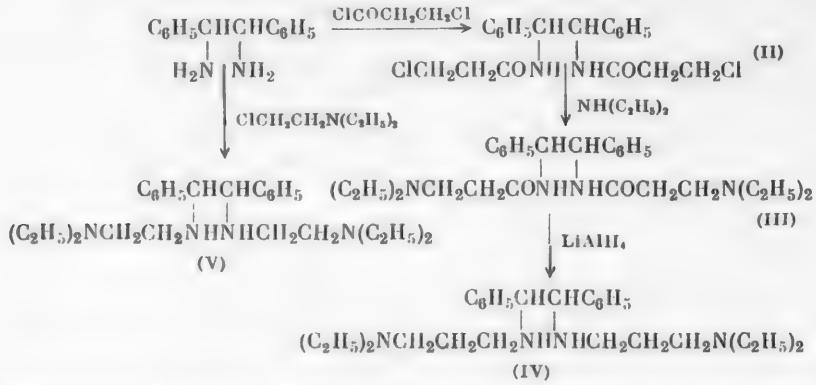
Some of the N-chloroacyl, N-dialkylaminoacyl, and N-dialkylaminoalkyl derivatives of aliphatic-aromatic amines we prepared previously [1,3] showed considerable physiological activity (action on the central nervous system).

In a previous communication [3] we described derivatives of this type, belonging to a series of amines with two phenyl nuclei (α,β-diphenylethylamine, α,β-diphenoxyethylamine, and their analogs). Continuing the search for physiologically active substances among derivatives of aliphatic-aromatic amines, we synthesized some previously unknown derivatives of α,β-diphenylethylenediamine of type (I).



(I)

We prepared racemic diphenylethylenediamine by catalytic hydrogenation of benzil dioxime over Raney nickel in 80% alcohol in the presence of caustic alkali (thus, the sodium salt of the dioxime was actually hydrogenated). This method gave considerably better results than other methods of preparing diphenylethylenediamine described previously [4]. N,N-substituted diphenylethylenediamines (I) were prepared according to the following scheme:



The bis-β-chloropropionyl derivative (II) was prepared by condensation of α,β-diphenylethylenediamine with β-chloropropionyl chloride in a two-phase system (ethyl acetate-water) in the presence of caustic alkali as we described previously [2] for the preparation of other analogous compounds. The diamide (II), which was a crystalline, high-melting substance, was then condensed with diethylamine by boiling the two reagents in pyridine, and the dialkylaminoalkyl-substituted diamide (III) was isolated as the hydrochloride. Reduction of (III) with lithium aluminum hydride gave a high yield of tetramine (IV). Its lower homolog with an ethylene chain (V) was obtained in about 50% yield by direct condensation of α,β-diphenylethylenediamine with diethylaminoethyl chloride in aqueous solution in the presence of bicarbonate.

Since the haloalkylates of the compounds obtained could also have been of interest from the point of view of physiological activity, two of the compounds described, namely, the diamide (III) and the tetramine (V), were converted into their bis-iodoalkylates by heating toluene solutions with ethyl iodide.

All the compounds obtained were tested for physiological activity by M. Yu. Ladinskaya. None of the compounds obtained showed antispasmodic activity, but all, apart from (II), showed appreciable curare-like action. The most active in this respect was the iodomethylate of tetramine (V), which produced relaxation of muscle for 7—10 minutes. It is interesting that tetramine (IV), which has no ammonium groupings, also had an appreciable action and completely relazed muscle for 4—5 minutes.

EXPERIMENTAL

α, β-Diphenylethylenediamine. To a suspension of 6 g of benzil dioxime in 110 ml of alcohol was added 1.2 g of sodium hydroxide in 20 ml of water and the mixture heated at 60—70° until the dioxime dissolved completely; 3—5 g of Raney nickel was added to the clear, hot solution, which was hydrogenated at normal pressure and room temperature for 2.5—3 hours, when the theoretical amount of hydrogen (2.3 liters) was absorbed. After removal of the nickel, the filtrate was concentrated to small volume in vacuum and the residue adjusted to pH 2—3 with 20% hydrochloric acid; for the removal of impurities, the suspension of the difficultly water-soluble hydrochloride was treated 2—3 times with ether, the ether which dissolved in the water removed, the suspension adjusted to pH 10—12 with alkali solution, the liberated yellow oil extracted with ether, and the ether extract dried with NaOH; to the dry ether solution of the base was added an ether solution of hydrogen chloride to precipitate the dihydrochloride as a white, amorphous powder (4.2 g, 60%), which crystallized from anhydrous alcohol as colorless, lustrous needles (m.p. 243—245°).

Found %: Cl 24.55, 24.63; C 58.34, 58.59; H 6.61, 6.76. $C_{14}H_{12}N_2Cl_2$. Calculated %: Cl 24.86; C 58.95; H 6.36.

The report that the dihydrochloride contains two molecules of water of crystallization [4] was not confirmed by our data.

N,N'-Bis-β-chloropropionyl-α,β-diphenylethylenediamine (II). A mixture of 3.2 g of α, β-diphenylethylenediamine hydrochloride and 40 ml of water was heated and stirred until solution was almost complete, and then 0.9 g of sodium hydroxide in 5 ml of water and 60 ml of ethyl acetate (free from acetic acid) was added to the solution with continuous stirring. The mixture was cooled to 4—6°, a further 0.9 g of sodium hydroxide in 10 ml of water added, and then 2.1 ml (2.88 g) of β-chloropropionyl chloride introduced dropwise with vigorous stirring; the pH was adjusted to 7.5—8.0 and then the reaction mixture was stirred at room temperature for 40—60 minutes. The colorless precipitate of diamide was collected, washed repeatedly with water, and dried to yield 3 g of product; a further 0.5 g of the substance was obtained from the ethyl acetate solution. The total yield was 3.5 g (80%).

Found %: Cl 17.74, 17.70; N 7.43, 7.36. $C_{20}H_{22}O_2Cl_2$. Calculated %: Cl 18.02; N 7.12.

The substance was insoluble in alcohol, ether, chloroform, dichloroethane, dioxane, acetone, and butanol, and sparingly soluble in pyridine and glacial acetic acid. On recrystallization from glacial acetic acid, it formed fine, colorless, lustrous crystals with m.p. 335—339° (decomp.).

N,N'-Bis-β-diethylaminopropionyl-α,β-diphenylethylenediamine (III). A mixture of 8.8 g of N,N'-bis-β-chloropropionyl-α,β-diphenylethylenediamine and 130 ml of pure pyridine was heated with stirring until the diamide dissolved. To the clear solution was added 30 ml of diethylamine and the mixture boiled for 2.5—3 hours. The slightly yellowish solution was cooled to 0°, the precipitate removed, the filtrate evaporated to dryness in vacuum, the residue dissolved in 17% hydrochloric acid, and the acid solution treated with ether and evaporated to dryness in vacuum; the glassy yellow residue was treated with anhydrous alcohol to form a colorless, crystalline precipitate of the dihydrochloride. Treatment of the alcohol mother solution with ether precipitated a further amount of the substance. After recrystallization from alcohol, it had m.p. 216—218°. The yield was 6.8 g (58%).

Found %: Cl 13.17, 13.22; N 10.19, 10.24. $C_{28}H_{44}O_2N_4Cl_2$. Calculated %: Cl 13.14; N 10.36.

The base, liberated from the dihydrochloride, formed colorless crystals, which were insoluble in water and ether; after recrystallization from 50% alcohol, it had m.p. 200—201°.

Found %: N 11.69, 11.17. $C_{28}H_{42}O_2N_4$. Calculated %: N 11.56.

Diiodoethylate of N,N'-bis-β-diethylaminopropionyl-α,β-diphenylethylenediamine. An aqueous solution of 1.2 g of N,N'-bis-β-diethylaminopropionyl-α,β-diphenylethylenediamine hydrochloride was treated with excess alkali, the liberated base extracted with toluene, 2 ml of ethyl iodide added to the dried toulene extract, and the mixture boiled for 2 hours; we obtained 1.2 g (70%) of colorless crystals, which were insoluble in toluene, anhydrous alcohol, acetone, and benzene; after recrystallization from 75% alcohol, they had m.p. 260—262° (decomp.).

Found %: I 32.52, 32.47; N 6.70, 6.83. $C_{32}H_{52}O_2N_4I_2$. Calculated %: I 32.60; N 7.19.

N,N'-Bis-diethylaminopropyl-α,β-diphenylethylenediamine (IV). To 0.5 g of lithium aluminum hydride in 150 ml of absolute ether was added a suspension of 2 g of N,N'-bis-β-diethylaminopropionyl-α, β-diphenylethylenediamine dihydrochloride in 150 ml of absolute ether and the mixture heated for 2 hours. The reaction product was decomposed with 30 ml of water, the ether layer separated, and the aqueous layer treated with alkali and extracted with ether. The ether extract was dried and treated with an ether solution of hydrogen chloride to precipitate the the tetrahydrochloride as colorless, hygroscopic crystals in a yield of 2 g (92%). After recrystallization from anhydrous alcohol with the addition of ether, the substance had m.p. 213—215°.

Found %: N 9.32, 9.28. $C_{28}H_{50}N_4Cl_4$. Calculated %: N 9.58.

N,N'-Bis-diethylaminoethyl-α,β-diphenylethylenediamine (V). A sample of 5 g of α,β-diphenylethylenediamine hydrochloride was dissolved in 80 ml of water with stirring and heating, and to the solution were added 3 g of sodium bicarbonate and 80 ml of alcohol; the mixture was stirred for 10—15 minutes, to the clear solution was added a further 9 g of sodium bicarbonate, 10 g of diethylaminoethyl chloride in 40 ml of water introduced slowly, the mixture stirred for 1.5 hours, the alcohol removed in vacuum, and 160 ml of water and excess alkali added to the residue; the oily base liberated was extracted with benzene, the benzene solution dried and treated with an ether solution of hydrogen chloride to precipitate the hygroscopic tetrahydrochloride, which was dried in vacuum to yield 4.5 g (46%) of product. After recrystallization from anhydrous alcohol with ether added, the substance formed colorless, lustrous crystals with m.p. 225—226°.

Found %: Cl 25.23, 25.09. $C_{26}H_{46}N_4Cl_4$. Calculated %: Cl 25.46.

Diiodoethylate of N,N'-bis-diethylaminoethyl-α,β-diphenylethylenediamine. To an aqueous solution of 0.9 g of N,N'-bis-diethylaminoethyl-α, β-diphenylethylenediamine hydrochloride was added excess alkali, the liberated base extracted with toluene, 1.5 ml of ethyl iodide added to the dried tuluene extract, and the mixture boiled for 2 hours. The diiodoethylate precipitated from the solution as lustrous, colorless crystals in a yield of 0.75 g (65%) and had m.p. 196-198°.

Found %: I 35.50, 35.68; N 7.65, 7.58. $C_{30}H_{52}N_4I_2$. Calculated %: I 35.26; N 7.75.

SUMMARY

N,N'-Bis-β-chloropropionyl, N,N'-bis-β-diethylaminopropionyl, N,N'-bis-diethylaminoethyl, and N,N'-bis-diethylaminopropyl derivatives of α,β-dithenylenediamine were prepared.

LITERATURE CITED

[1] N. K. Kochetkov and N. V. Dudykina, Zhur. Obshchei Khim. 26, 2612 (1956).*

[2] N. K. Kochetkov and N. V. Dudykina, Zhur. Obshchei Khim. 27, 1399 (1957).*

[3] N. K. Kochetkov and N. V. Dudykina, Zhur. Obshchei Khim. 29, 1659 (1959).*

[4] F. Feist, Ber. 27, 214 (1894).

*Original Russian pagination. See C. B. translation.

REACTIONS OF DI-AND TRIFUNCTIONAL ALKYLALKOXYSILANES WITH PHOSPHORUS PENTOXIDE

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Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4082–4085, December, 1959

Original article submitted December 2, 1958

Alkyalkoxysilanes can react with PCl_3 [1,2], PBr_3 [2-5], PCl_5 [6-7], $POCl_3$ [2,8] and H_3PO_4 [9]. The reaction of alkylalkoxysilanes with P_2O_5 has not been described in the literature.

The present work is a continuation of our investigations of the reaction of tetraalkoxysilanes with $POCl_3$, PCl_3 [10], also with P_2O_5 [11], and the possibility of practical application of some of the compounds obtained [12]. In the present work we investigated the reaction of di- and trifunctional alkylalkoxysilanes with phosphorus pentoxide. We established that difunctional alkylalkoxysilanes react with P_2O_5 acoording to the following scheme:

$$3nR_2Si(OR')_2 + nP_2O_5 \rightarrow [Si_3P_2O_8R_6]_n + 3nR_2'O,$$

where $R = CH_3$, C_2H_5; $R' = C_2H_5$, a $-C_4H_9$.

In this case we isolated two polymeric compounds: $[Si_3P_2O_8(CH_3)_6]_n$ from $(CH_3)_2Si(OC_2H_5)_2$ or $(CH_3)_2Si(OC_4H_9)_2$ and P_2O_5 and $[Si_3P_2O_8(C_2H_5)_6]_n$ from $(C_2H_5)_2Si(OC_2H_5)_2$ and P_2O_5. The first of these products (dimethylpolysiloxane phosphate) was synthesized previously by M. G. Voronkov and V. N. Zgonnik by reaction of R_2SiX_2 or $RSiX_3$ (where X is halogen or OCH_3) with solid phosphoric acid [13]. Trifunctional alkylalkoxysilanes reacted with phosphorus pentoxide according to the following scheme:

$$2nRSi(OR')_3 + nP_2O_5 \longrightarrow [RSi(OR')_2OP_2O_4OSi(OR')_2R]_n + nR_2'O,$$

where $R = CH_3$, C_2H_5; $R' = C_2H_5$.

In this case we isolated two new polymeric organosilicon substances: $[Si_2P_2C_{10}H_{26}O_{10}]_n$ and $[Si_2P_2C_{12}H_{30}O_{10}]_n$.

EXPERIMENTAL *

The starting materials for the present investigation were dimethyldiethoxysilane, dimethyldibutoxysilane, diethyldiethoxysilane, methyltriethoxysilane, and ethyltriethoxysilane. Dimethyldi-n-butoxysilane was synthesized by a procedure described in the literature [14]. The other alkylalkoxysilanes were obtained by a method based on the reaction of aniline with appropriate alkylchlorosilanes and subsequent reaction of the anilides obtained, $R_nSi(NHC_6H_5)_{4-n}$ with an appropriate anhydrous alcohol [15]. The yield of alkylalkoxysilanes was 70-80%. The physical constants of the starting substances agreed well with literature data (see table).

Reaction of dimethyldiethoxy- or dimethyldi-n-butoxysilane with phosphorus pentoxide. Into a 100-ml round-bottomed flask, fitted with a reflux condenser, was placed 0.15 mole of freshly prepared dimethyldialkoxysilane. Then 0.05 mole of P_2O_5 was gradually added over a period of 15–20 minutes. After addition of the P_2O_5, the mixture was heated to boiling on an oil bath and boiled for 2.5–3 hours. When $(CH_3)_2Si(OC_2H_5)_2$ was used, distillation

* The students Yu. P. Znamenskii and V. N. Il'in participated in the experimental part of the work.

of the reaction mixture yielded fractions containing diethyl ether, the slight excess of the original $(CH_3)_2Si(OC_2H_5)_2$, and also phosphoric acid derivatives. At 170° there was slight frothing in the flask and the formation of a clear, yellowish liquid mass, which changed to a gluey substance on cooling. When $(CH_3)_2Si(OC_4H_9\text{-}n)_2$ was used, distillation of the reaction mixture yielded fractions containing di-n-butyl ether, excess of the original $(CH_3)_2Si(OC_4H_9)_2$ (185—189°), and a mixture of phosphorus-silicoorganic compounds. At 260—270° frothing was observed in the distillation flask and the formation of a clear, yellowish, gluey substance. The fractions containing the corresponding ethers were redistilled with a fractionating column and identified (diethyl ether b.p. 35—36°, d_4^{20} 0.7203 and dibutyl ether: b.p. 141—142°, d_4^{20} 0.711, n_D^{18} 1.4030). The phosphorus-silicoorganic polymers were purified by heating with excess anhydrous benzene, which extracted the benzene-soluble impurities from the mixture.

The residue was dried in a drying cupboard at 120—130°. The substances obtained contained silicon, phosphorus, carbon, hydrogen, and oxygen. The phosphorus was determined according to the procedure in [10], silicon according to the procedure in [16], and carbon and hydrogen according to the procedure in [17, 18]. Analyses showed that the two substances obtained were identical in composition.

Found %: P 17.32, 17.05; Si 22.85, 22.70; C 19.50, 20.08; H 5.50, 5.39. $C_6H_{18}O_8P_2Si_3$. Calculated %: P 17.00; Si 23.12; C 19.77; H 4.98.

The substance obtained was found to be dimethylpolysiloxane phosphate with the composition $\{[(CH_3)_2Si]_3(PO_4)_2\}_n$. The molecular weight was determined by Rast's method with benzoic acid used as solvent. According to these determinations, the product investigated had a molecular weight of 2550 ($n \approx 7$).

Dimethylpolysiloxane phosphate was difficultly soluble in organic solvents (apart from benzoic acid and acetone), but under prolonged heating with water it was appreciably hydrolyzed and dissolved. When the product was heated with P_2O_5, it formed a solid substance with the composition $Si(PO_3)_4$. Further heating of dimethylpolysiloxane phosphate to 250° led to frothing and decomposition.

Reaction of diethyldiethoxysilane with phosphorus pentoxide. Into a 50-ml round-bottomed flask, fitted with a reflux condenser, was placed 12.1 ml (0.06 mole) of $(C_2H_5)_2Si(OC_2H_5)_2$ and 2.84 g (0.02 mole) of P_2O_5 gradually introduced over a period of 15—20 minutes. When the P_2O_5 was added, the mixture evolved heat. The reaction mixture was then heated to boiling on an oil bath and boiled for 2.5-3 hours. Distillation of the reaction mixture yielded fractions containing diethyl ether and a mixture of phosphorus-silicoorganic compounds. At 190° there remained in the distillation flask a yellow liquid, which frothed on further heating and thickened to a viscous gluey mass on cooling. It was purified by washing with hot anhydrous benzene and dried at 120—130°. Analyses of the purified material gave the following results.

Found %: P 13.52, 14.08; Si 18.62, 18.96; C 32.40, 31.70; H 7.06, 6.95. $C_{12}H_{30}O_8P_2Si_3$. Calculated %: P 13.81; Si 18.76; C 32.13; H 6.74.

Thus, the gluey substance obtained was found to be diethylpolysiloxane phosphate $\{[(C_2H_5)_2Si]_3(PO_4)_2\}_n$. The solubility of diethylpolysiloxane phosphate in organic solvents was slightly higher than that of the methyl derivative. Determination of the molecular weight by Rast's method with benzoic acid gave the value $n \approx 4$ (3.81 and 3.94).

Diethyl ether was isolated from the fractions containing it and identified. The absence of alkoxyl groups from the dimethyl or diethylpolysiloxane phosphates was demonstrated by qualitative reactions for these groups described in [19].

Reaction between methyltriethoxy- or ethyltriethoxysilane and phosphorus pentoxide. Into a 50-ml round-bottomed flask, fitted with a reflux condenser, was placed 0.1 mole of the appropriate alkyltriethoxysilane. Then 0.05 mole of P_2O_5 was added gradually over a period of 20—25 minutes. The mixture obtained was heated to boiling on an oil bath and boiled for 2 hours. White precipitates formed in both cases, and these were separated by means of a Buchner funnel. Diethyl ether was distilled from the mother liquor and identified. The white precipitates obtained were transferred to a filter and washed with hot anhydrous benzene and then dried in a drying cupboard at 150—160°. The substances obtained were analyzed by the methods mentioned above. The ethoxyl group content of the products obtained was determined by a semimicro method [20]. The analyses gave the following results.

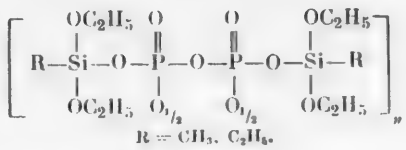
A) Substance obtained by reaction of methyltriethoxysilane with phosphorus pentoxide.

Found %: P 13.91, 14.24; Si 13.01, 13.58; C 27.96, 28.25; H 5.51, 5.78; OC_2H_5 41.82, 42.04, $C_{10}H_{26}O_{10}P_2Si_2$. Calculated %: P 14.59; Si 13.23; C 28.30; H 6.17; OC_2H_5 42.47.

B) Substance obtained by reaction of ethyltriethoxysilane with phosphorus pentoxide.

Found %: P 13.41, 13.28; Si 12.82; C 32.54, 31.72; H 6.06, 6.31; OC_2H_5 40.30, 39.41. $C_{12}H_{30}O_{10}P_2Si_2$. Calculated %: P 13.69; Si 12.41; C 31.85; H 6.68; OC_2H_5 39.83.

The substances obtained had a high degree of polymerization (we could not determine their molecular weight due to their low solubility in organic solvents) and apparently had the following structure:



R = CH_3, C_2H_5.

Investigation of the infrared spectra of the phosphorus-silicoorganic compounds obtained confirmed the given structure.

Formula of substance	Boiling point	d_4^{20}	n_D^{20}
$(CH_3)_2Si(OC_2H_5)_2$	111—112°	0.893	1.3860
$(CH_3)_2Si(OC_4H_9)_2$	187—188	0.847	1.4060
$(C_2H_5)_2Si(OC_2H_5)_2$	154—155	0.8732	1.4020
$CH_3Si(OC_2H_5)_3$	150—151	0.941	1.3874
$C_2H_5Si(OC_2H_5)_3$	158—159	0.9211	1.3858

SUMMARY

1. The reactions of dimethyldiethoxy-, dimethyldi-n-butoxy-, diethyldiethoxy-, methyltriethoxy-, and ethyltriethoxysilanes with phosphorus pentoxide were investigated. These reactions were accompanied by dealkoxylation processes, leading to the formation of phosphorus-silicoorganic substances and ethers.

2. A new method was developed for preparing polymeric compounds of the type $[Si_3P_2O_8R_6]_n$ and $[Si_2P_2O_6R_2(OR')_4]_n$.

3. The following three polymeric compounds, which have not been described in the literature, were prepared: $[Si_3P_2O_8(C_2H_5)_6]_n$, $[Si_2P_2O_6(CH_3)_2(OC_2H_5)_4]_n$ and $[Si_2P_2O_6(C_2H_5)_2(OC_2H_5)_4]_n$.

LITERATURE CITED

[1] C. Friedel and A. Ladenburg, Ber. 3, 15 (1870).

[2] J. Fertig, W. Gerrard and H. Herbst, J. Chem. Soc. 1488 (1957).

[3] W. F. Gilliam, R. N. Meals and R. O. Sauer, J. Am. Chem. Soc. 68, 1181 (1946).

[4] P. A. McCusker and E. L. Reilly, J. Am. Chem. Soc. 75, 1583 (1953).

[5] L. H. Sommer, H. D. Blankman and P. C. Miller, J. Am. Chem. Soc. 76, 803 (1954).

[6] E. Larsson and B. Smith, Svensk Kem. Tid. 62, 87 (1950); C. A. 44, 7224 (1950).

[7] U. S. Pat. 2386488; C. A. 40, 592 (1946).

[8] J. Fertig and W. Gerrard, Chem. and Ind. No. 3, 83 (1956).

*Original Russian pagination. See C. B. translation.

[9] M. G. Voronkov, V. A. Kolesova and V. N. Zgonnik, Izvest. Akad. Nauk. SSSR, Otdel. Khim. Nauk, 1363 (1957). •

[10] A. P. Kreshkov and D. A. Karateev, Zhur. Obshchei Khim. 27, 2715 (1957). •

[11] A. P. Kreshkov and D. A. Karateev, Zhur. Priklad. Khim. 30, 1416 (1957). •

[12] A. P. Kreshkov, V. I. Khramova and D. A. Karateev, Author's Certificate No. 113143 (1958).

[13] M. G. Voronkov and V. N. Zgonnik, Zhur. Obshchei Khim. 27, 1483 (1957). •

[14] R. O. Sauer, J. Am. Chem. Soc. 68, 138 (1946).

[15] A. P. Kreshkov, L. V. Myshlyaeva and L. M. Khananashvili, Zhur. Obshchei Khim. 28, 2112 (1958)•; A. P. Kreshkov, L. V. Myshlyaeva and L. M. Khananashvili, Author's Certificate No. 108137 (1957).

[16] K. A. Andrianov, B. N. Rutovskii and A. A. Kazakova, Zhur. Obshchei Khim. 26, 267 (1956). •

[17] V. A. Klimova, M. O. Korshun and E. G. Bereznitskaya, Zhur. Anal. Khim 11, 223 (1956). •

[18] V. A. Klimova, M. O. Korshun and E. G. Bereznitskaya, Doklady Akad. Nauk SSSR, 96, 287 (1954).

[19] A. P. Kreshkov, V. A. Bork, L. V. Myshlyaeva and G. D. Nessonova, Analysis of Organosilicon Compounds [in Russian] (State Chemistry Press, Moscow, 1954), p. 118.

[20] A. P. Kreshkov and G. D. Nessonova, Zhur. Anal. Khim. 4, 220 (1949).

•Original Russian pagination. See C. B. translation.

DERIVATIVES OF N-PHOSPHORIC ACIDS OF NITROBENZENESULFONAMIDES

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Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4085–4091, December, 1959

Original article submitted December 17, 1958

Up to the present time, the reaction of aryl trichlorophosphazosulfones and diacid chlorides of arenesulfonamidophosphoric acids [1] with primary and secondary amines has been studied on the example of ammonia and aromatic amines [2]. It seemed interesting to study this reaction with secondary acyclic amines. As examples we chose nitrophenyl trichlorophosphazosulfones [3] and diacid chlorides of nitrobenzenesulfonamidophosphoric acids [3] and dimethyl- and diethylamines.

o-, m- and p-nitrophenyl trichlorophosphazosulfones reacted with aqueous solutions of dialkylamines to form a mixture of products that was very difficult to separate. During the action of anhydrous dimethyl- and diethyl amines on nitrophenyl trichlorophosphazosulfones in benzene solution, the chlorine atoms were readily replaced by dialkylamino groups, but in the case of dimethylamine all three chlorine atoms exchanged to give good yields of nitrophenyl hexamethyltriamidophosphazosulfones according to the scheme:

$$NO_2C_6H_4SO_2N{=}PCl_3 + 6NH(CH_3)_2 \longrightarrow 3(CH_3)_2NH_2Cl + \\ + NO_2C_6H_4SO_2N{=}P[N(CH_3)_2]_3,$$

and in the case of diethylamine only two chlorine atoms reacted to form nitrophenyl tetraethyldiamidomonochlorophosphazosulfones according to the scheme:

$$NO_2C_6H_4SO_2N{=}PCl_3 + 4NH(C_2H_5)_2 \longrightarrow 2(C_2H_5)_2NH_2Cl + \\ + NO_2C_6H_4SO_2N{=}PCl[N(C_2H_5)_2]_2$$

The third chlorine atom was not replaced by a diethylamino group even with 40 hours boiling with a large excess of diethylamine in benzene and did not react with caustic alkalis during prolonged boiling in aqueous alcohol solutions.

The stability of the chlorine atom in nitrophenyl tetraethyldiamidomonochlorophosphazosulfones to hydrolysis and amidation is undoubtedly explained by steric factors, arising from the greater volume of the diethylamino groups as compared with dimethylamino groups.

Nitrophenyl hexamethyltriamidophosphazosulfones (I) were colorless, crystalline substances (Table 1) of neutral character, which were insoluble in aqueous solutions of mineral acids and caustic alkalis. The ortho-nitro isomer of (I) was not hydrolyzed by boiling with either 0.3–2.0 N aqueous alcoholic alkali or 0.3–2.0 N aqueous alcoholic acid. When boiled with 0.3 N aqueous alcoholic alkali, the meta- and para-isomers of (I) were hydrolyzed to give a mixture of products from which it was possible to isolate the starting materials, tetramethyldiamides of the corresponding nitrobenzensulfonamidophosphoric acids (see below), and the corresponding nitrobenzenesulfonamides. The stability of the ortho-isomer to hydrolysis is undoubtedly explained by steric factors, i.e., the proximity of the nitro group.

Nitrophenyl tetraethyldiamidomonochlorophosphazosulfones (II) were colorless, crystalline substances of neutral character (Table 1), melting considerably lower than the corresponding (I). The meta-nitro isomer of (II) was

TABLE 1

Nitrophenyl Hexamethyltriamidophosphazosulfones of the Type $NO_2C_6H_4SO_2N{=}P[N(CH_3)_2]_3$ (I) and Nitrophenyl Tetraethyldiamidomonochlorophosphazosulfones of the Type $NO_2C_6H_4\text{-}SO_2N{=}PCl[N(C_2H_5)_2]_2$ (II)

Type	Position of NO_2	Yield (in %)	Melting point	Found, %	Empirical formula	Calc.	Solubility**					
							alcohol	ether	ligroin	acetone	benzene	CCl_4
(I)	o	86	160–163°	N 18.84	$C_{12}H_{22}O_4N_5SP$	N 19.29	+	=	=	+	+	+
	m	76	66–68	P 8.49	$C_{12}H_{22}O_4N_5SP$	P 8.54	+	=	=	+	+	+
	p	79	109–111	P 8.58, *M* 360 *	$C_{12}H_{22}O_4N_5SP$	P 8.54, *M* 363	+	=	=	+	+	+
(II)	o	99	84–86	Cl 8.70	$C_{14}H_{24}O_4N_4SPCl$	Cl 8.64	+	–	–	+	+	+
	p	98	58–60	Cl 8.76	$C_{14}H_{24}O_4N_4SPCl$	Cl 8.64	+	+	=	+	+	+

*By Rast's method.

**Symbols: = insoluble at boiling point; –difficultly soluble at boiling point; + difficultly soluble at 20°, but readily soluble at boiling point; ++ readily soluble at 20°. All the substances were insoluble in boiling water.

obtained as an oily liquid, which could not be purified or crystallized.

The chlorine atom in the molecule of (II) was firmly bound and was not hydrolyzed even by boiling for 3 hours with an aqueous alcohol solution of caustic alkali.

The tetramethyldiamides of m- and p-nitrobenzenesulfonamidophosphoric acids could be obtained in low yields by alkaline hydrolysis of the corresponding (I) (see above) according to the scheme:

$$NO_2C_6H_4SO_2N{=}P[N(CH_3)_2]_3 + H_2O \longrightarrow NH(CH_3)_2 + \\ + NO_2C_6H_4SO_2NHPO[N(CH_3)_2]_2$$

The ortho-isomer of the tetramethyldiamide and the tetraethyldiamides of nitrobenzenesulfonamidophosphoric acids (from II) could not be obtained in this way. The tetraalkyldiamides of nitrobenzenesulfonamidophosphoric acids (III) could be obtained readily in good yields from the diacid chlorides of nitrobenzenesulfonamidophosphoric acids and the corresponding dialkylamines. In this case, the readily water-soluble dialkylammonium salts were first formed and on acidification, these gave the water-insoluble free (III) according to the scheme:

$$NO_2C_6H_4SO_2NHPOCl_2 + 5NHR_2 \longrightarrow$$
$$\longrightarrow 2NH_2R_2Cl + [NO_2C_6H_4SO_2NPO(NR_2)_2]^-[NH_2R_2]^+ \xrightarrow{+H^+}$$
$$\longrightarrow NO_2C_6H_4SO_2NHPO(NR_2)_2$$

However, the tetraethyldiamide of o-nitrobenzenesulfonamidophosphoric acid could not be obtained in a pure state by this method either, and this was probably due to steric factors (ortho position of the nitro group). Substances (III) were colorless, crystalline materials of acid character (Table 2), melting higher than the corresponding (I), dissolving readily in aqueous solutions of caustic alkalis and carbonates, and titrating as monobasic acids. They all crystallized from alcohol as fine prisms.

For studying the physiological properties, we prepared the sodium salts of the diesters of nitrobenzenesulfonamidophosphoric acids of type $[NO_2C_6H_4SO_2NPO(OR)_2]^-Na^+$ (IV). These salts could be obtained from free diesters of nitrobenzenesulfonamidophosphoric acids [4] and sodium hydroxide or sodium carbonate, but it was more

TABLE 2

Tetraalkyldiamides of Nitrobenzenesulfonamidophosphoric Acids of the Type $NO_2C_6H_4$-$SO_2NHPO(NR_2)_2$ (III)

Position of NO_2	R	Yield (in %)	Melting point	Found % N	Found equiv	Empirical formula	Calculated* % N	Solubility** water	alcohol	ligroin	acetone	benzene	CCl_4
o	CH_3	82	161—164°	16.63	1.003	$C_{10}H_{17}O_5N_4SP$	16.66	+	+	=	+	=	=
m	CH_3	82	145—147	16.50	1.002	$C_{10}H_{17}O_5N_4SP$	16.66	—	+	=	++	=	=
p	CH_3	84	169—170	16.73	0.975	$C_{10}H_{17}O_5N_4SP$	16.66	—	++	=	+	—	=
m	C_2H_5	79	125—127	14.41	1.010	$C_{14}H_{25}O_5N_4SP$	14.36	—	++	=	++	+	—
p	C_2H_5	83	109—111	14.08	0.980	$C_{14}H_{25}O_5N_4SP$	14.36	=	+	—	++	+	=

*The calculated equivalent for all the compounds was 1.000.

**All the substances were insoluble in boiling ether.

convenient and rapid to prepare them directly from diacid chlorides of nitrobenzenesulfonamidophosphoric acids and the corresponding sodium alcoholates or arylates according to the scheme:

$$NO_2C_6H_4SO_2NHPOCl_2 + 3NaOR \longrightarrow ROH + 2NaCl + [NO_2C_6H_4SO_2NPO(OR)_2]^-Na^+$$

The substances (IV) were colorless, crystalline materials with the characteristics of neutral salts of strong acids. They dissolved readily in water, alcohol and acetone, and crystallized readily as needles from alcohol or a very small amount of water. Their aqueous solutions were neutral to phenolphtahlein and, on acidification with mineral acids, deposited the water-insoluble free diesters of arenesulfonamidophosphoric acids. It is interesting to note that the sodium salts of the di-p-chlorodiphenyl esters of nitrobenzenesulfonamidophosphoric acids were almost completely extracted from aqueous solutions by ether and also were appreciably soluble in benzene and carbon tetrachloride. The sodium salts of all the other diesters were not extracted from aqueous solutions by ether and were insoluble in nonpolar solvents. The sodium salts of some diesters crystallized with two and three molecules of water of crystallization (see Table 3).

EXPERIMENTAL

Nitrophenyl hexamethyltriamidophosphazosulfones (I). With vigorous stirring and cooling in ice water, a solution of 0.05 mole of nitrophenyl trichlorophosphazosulfone in 200 ml of benzene was treated with dry, gaseous dimethylamine at such a rate that the temperature of the reaction mixture did not exceed 40°. A precipitate of dimethylamine hydrochloride and (I) formed immediately. When 0.3 mole of dimethylamine has been absorbed (check by increase in weight), the benzene was removed in vacuum at 30-40° and the solid residue washed with small amounts of water to removed dimethylamine hydrochloride. The substances were purified by recrystallization from small amounts of alcohol (fine prisms).

Nitrophenyl tetraethyldiamidomonochlorophosphazosulfones (II). With vigorous stirring, 0.08 mole of diethylamine was added slowly from a dropping funnel to a solution of 0.02 mole of nitrophenyl trichlorophosphazosulfone in 80 ml of benzene. The reaction was accompanied by strong evolution of heat. When the whole of the diethylamine had been added, the mixture was boiled under reflux for 8 hours and then the diethylamine hydrochloride was removed and the filtrate evaporated to dryness in vacuum. The residue consisted of crystals or oily liquids which rapidly crystallized. The ortho-nitro isomer was recrystallized from alcohol and the para-nitro isomer from a mixture of benzene and ligroin; both substances crystallized as fine prisms.

In other experiments twice as much diethylamine (0.16 mole) was taken and boiling was continued for 40 hours, but the results were the same.

TABLE 3

Sodium Salts of Diesters of Nitrobenzenesulfonamidophosphoric Acids of Type $[NO_2C_6H_4SO_2NPO(OR_2)_2]^- Na^+$ (IV).

R	Pos. of NO_2	Yield (in %)	Melting point	Water of crystallization content	Found,* % N	Empirical formula**	Calc.,* % N
CH_3	o ***	70	156–158°	None	8.52	$C_8H_{10}O_7N_2SPNa$	8.43
	m	79	195–198	$2H_2O$	8.61	$C_8H_{10}O_7N_2SPNa$	8.43
	p	83	188–190	$2H_2O$	8.58	$C_8H_{10}O_7N_2SPNa$	8.43
C_6H_5	o	76	164–167	$3H_2O$	6.25	$C_{18}H_{14}O_7N_2SPNa$	6.14
	m ****	82	137–140	$3H_2O$	6.17	$C_{18}H_{14}O_7N_2SPNa$	6.14
	p	94	210–212	None	6.30	$C_{18}H_{14}O_7N_2SPNa$	6.14
p-ClC_6H_4	o	64	182–184	$3H_2O$	5.39	$C_{18}H_{12}O_7N_2Cl_2SPNa$	5.33
	m	59	153–155	$3H_2O$	5.37	$C_{18}H_{12}O_7N_2Cl_2SPNa$	5.33
	p	87	221–222	None	5.40	$C_{18}H_{12}O_7N_2Cl_2SPNa$	5.33
o-$NO_2C_6H_4$	o	92	200–202	same	10.30	$C_{18}H_{12}O_{11}N_4SPNa$	10.26
	m	90	172–174	»	10.23	$C_{18}H_{12}O_{11}N_4SPNa$	10.26
	p	88	202–205	»	10.31	$C_{18}H_{12}O_{11}N_4SPNa$	10.26
p-$NO_2C_6H_4$	o	87	210–213	»	10.29	$C_{18}H_{12}O_{11}N_4SPNa$	10.26
	m	87	216–218	»	10.22	$C_{18}H_{12}O_{11}N_4SPNa$	10.26
	p	83	220–222	»	10.21	$C_{18}H_{12}O_{11}N_4SPNa$	10.26

*Determined by drying at 4 mm and 80° for 3–4 hours.

**For anhydrous salts.

***Very readily soluble in water.

****Comparatively difficultly soluble in water.

Hydrolysis of m- and p-nitrophenyl hexamethyltriamidophosphazosulfones. After boiling a mixture of 0.01 mole of m- or p-nitrophenyl hexamethyltriamidophosphazosulfone, 25 ml of ethanol, and 33.3 ml of 0.3 N aqueous sodium hydroxide solution for 1 hour, we isolated 25 and 21% of the starting materials, 61 and 63% of the tetramethyldiamides of m- and p-nitrobenzenesulfonamidophosphoric acids, and about 3% of m- and p-nitrobenzenesulfonamides. After o-nitrophenyl hexamethyltriamidophosphazosulfone had been boiled for many hours with alkali, the substance was recovered unchanged practically quantitatively.

Tetramethyldiamides of nitrobenzenesulfonamidophosphoric acids. (III). With vigorous stirring and cooling in an ice-salt mixture, a solution of 0.1 mole of the diacid chloride of nitrobenzenesulfonamidophosphoric acid in 25 ml of dioxane was added to 30 ml of a 33% aqueous solution of dimethylamine at such a rate that the temperature of the reaction mixture did not exceed 25°. The mixture was then evaporated to a volume of about 5 ml in vacuum at 30° and 2 ml of 5 N hydrochloric acid added. The crystalline precipitate was collected, washed with ether and water, dried in air, and recrystallized from a small amount of alcohol (fine prisms).

Tetraethyldiamides of nitrobenzenesulfonamidophosphoric acids (III). To a solution of 0.01 mole of the diacid chloride of nitrobenzenesulfonamidophosphoric acid in 20 ml of dioxane was added a solution of 0.05 mole of diethylamine in 15 ml of dioxane at such a rate that the temperature of the reaction mixture did not exceed 25°. When all the diethylamine had been added, the mixture was stirred for 4 hours at room temperature, the dioxane then evaporated in vacuum at 30°, 5 ml of 2 N hydrochloric acid added to the residue, and the mixture again evaporated in vacuum. The second evaporation in vacuum was necessary for complete removal of the dioxane, as the tetraethyldiamides precipitated as uncrystallizable oils in the presence of dioxane. After evaporation, 3–5 ml of water was added to the residue. The tetraethyldiamides precipitated as oils which rapidly crystallized. They were purified by recrystallization from small amounts of alcohol (fine prisms).

Sodium salts of dimethyl esters of nitrobenzenesulfonamidophosphoric acids (IV). With vigorous stirring and cooling in ice water, 0.02 mole of finely powdered acid chloride of nitrobenzenesulfonamidophosphoric acid was

added to a solution of 0.06 mole of sodium methylate in 35 ml of methanol at such a rate that the temperature of the reaction mixture did not exceed 35°, and then the mixture was boiled under reflux for 10 minutes and the methanol completely removed in vacuum at 30—40°. The residual dry crystalline powder consisted of sodium chloride and the sodium salts of the dimethyl esters. In the case of the m- and p-nitro isomers, the residue was treated with 5 ml of cold water to dissolve the sodium chloride and the residual sodium salt was collected and recrystallized from alcohol. The sodium salt of the o-nitro isomer was extremely readily soluble in water and therefore it was extracted from the dry residue after the methanol had been evaporated with 3—5 ml of boiling ethanol.

Sodium salts of diaryl esters of nitrobenzenesulfonamidophosphoric acids (IV). A solution of 0.02 mole of the diacid chloride of nitrobenzenesulfonamidophosphoric acid in 40 ml of dioxane was added with stirring to 0.06 mole of carefully dried and powdered sodium arylate. When the evolution of heat was complete, the mixture was boiled under reflux with stirring for an hour in the case of sodium salts of diphenyl esters, 3 hours in the case of di-p-chlorodiphenyl ester, and 6 hours in the case of dinitrodiphenyl esters. The dioxane was then removed in vacuum and 7—10 ml of cold water added to the residue. Two layers were formed—an aqueous solution of sodium chloride and a liquid mixture of the sodium salt of the diester with the corresponding phenol. The aqueous layer was separated and the liquid mixture treated 2—3 times with small amounts of ether (5—10 ml) to remove the corresponding phenol. The precipitated sodium salts were collected, washed with ether, and recrystallized from alcohol, with the exception of the sodium salt of the diphenyl ester of m-nitrobenzenesulfonamidophosphoric acid, which was recrystallized from water.

SUMMARY

1. By the action of dimethylamine on nitrophenyl trichlorophosphazosulfones, all three chlorine atoms were replaced by dimethylamino groups and nitrophenyl hexamethyltriamidophosphazosulfones were formed.

2. Only two chlorine atoms were replaced by diethylamino groups by the action of diethylamine on nitrophenyl trichlorophosphazosulfones and nitrophenyl tetraethyldiamidomonochlorophosphazosulfones were formed.

3. The ortho-isomer of the nitrophenyl hexamethyltriamidophosphazosulfones was not hydrolyzed by acids and alkalis, while the meta- and para-isomers were hydrolyzed with much more difficulty than in the case of most known phosphazosulfone compounds.

4. In contrast to all known chlorophosphazo compounds, nitrophenyl tetraethyldiamidomonochlorophosphazosulfones were not hydrolyzed by alkalis.

5. The action of dimethyl- and diethylamines on diacid chlorides of nitrobenzenesulfonamidophosphoric acids formed tetraethyldiamides of nitrobenzenesulfonamidophosophoric acids with the characteristics of strong monobasic acids.

6. The action of sodium methylate and arylates on diacid chlorides of nitrobenzenesulfonamidophosphoric acids yielded sodium salts of diesters of nitrobenzenesulfonamidophosphoric acids.

LITERATURE CITED

[1] A. V. Kirsanov, Zhur. Obshchei Khim. 22, 269 (1952);* A. V. Kirsanov and E. A. Abrazhanova, Zhur. Obshchei Khim., Coll. II, 1048 (1953).

[2] A. V. Kirsanov and E. A. Abrazhanova, Zhur. Obshchei Khim. Coll. II, 1059, 1370 (1953); A. V. Kirsanov and N. L. Egorova, Zhur. Obshchei Khim. 28, 1587 (1958).*

[3] A. V. Kirsanov and N. G. Feshchenko, Zhur. Obshchei Khim. 27, 2817 (1958).*

[4] A. V. Kirsanov and N. G. Feshchenko, Zhur. Obshchei Khim. 28, 339 (1958).*

*Original Russian pagination. See C. B. translation.

SYNTHESIS OF UNSYMMETRICAL AZINES

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Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp 4091–4093, December, 1959

Original article submitted July 6, 1959

In recent years there has been an increase in interest in a little-studied group of organic compounds, namely unsymmetrical azines: aldazines R–CH=N–N=CH–R_1 and ketazines $\begin{matrix} R \\ R \end{matrix}\!\!>\!C=N-N=C\!<\!\!\begin{matrix} R_1 \\ R_1 \end{matrix}$. These compounds were prepared first by Curtius and his co-workers [1], and later by other investigators [2–5], by the action of aldehydes or ketones on hydrazones.

$$R-\underset{\underset{H(R)}{|}}{C}=N-NH_2 + OC-\underset{\underset{H(R)}{|}}{R_1} \longrightarrow R-\underset{\underset{H(R)}{|}}{C}=N-N=\underset{\underset{H(R)}{|}}{C}-R_1 + H_2O$$

S. A. Tebinov [6] described the preparation of benzfurfuralazine, benzacetalazine, and furfuracetalazine by the addition of a mixture of the two aldehydes to an aqueous solution of hydrazine hydrate. In the opinion of the authors, the reaction proceeded according to the following scheme:

$$R-CHO + H_2N-NH_2 + OCH-R_1 \longrightarrow R-CH=N-N=CH-R_1 + H_2O$$

Despite many experiments according to Tebinov's procedure and other variations, in our work we were unable to obtain mixed (unsymmetrical) azines in a pure form by the direct action of hydrazine hydrate on a mixture of two aldehydes. Thus, the action of hydrazine hydrate on a mixture of benzaldehyde and acetaldehyde yielded two azines, namely, the azine from benzaldehyde in about 90% yield and the azine from acetaldehyde in about 40% yield, but no mixed azine. Similar results were obtained by the action of hydrazine hydrate on a mixture of benzaldehyde and isobutyraldehyde and of benzaldehyde and isovaleraldehyde. A mixture of benzaldehyde and furfural yielded a mixture of three azines, namely benzalazine, furfuralazine, and the mixed azine, but it was extremely difficult to separate them due to the similarity of their properties.

After hydrazine hydrate treatment of two aliphatic aldehydes of similar structure, for example, isobutyraldehyde and isovaleraldehyde, it was possible to isolate liquids giving similar analytical data to the expected mixed azine, but these liquids distilled over a wide range, even at low pressure, and did not have definite constants. The formation of small amounts of substances similar to mixed azines was observed during the action of hydrazine hydrate on a mixture of acetaldehyde and isobutyraldehyde and of acetaldehyde and isovaleraldehyde.

Data have recently appeared in the literature on the impossibility of preparing mixed azines by the action of acetaldehyde and formaldehyde on cyclohexanone hydrazone [5].

In the light of the facts presented, the results of Tebinov's experiments must be regarded as inaccurate. This conclusion is confirmed by the facts that benzfurfuralazine obtained by Barany [9] had m.p. 63–64° instead of 99–100° as reported by Tebinov [6] and the benzacetalazine we synthesized was a liquid which did not solidify when cooled to -15° and not crystals with m.p. 89–90°, as reported by the above author.

Benzacetalazine was readily obtained by the action of acetaldehyde on benzylidenehydrazine (benzaldehyde hydrazone), which in its turn was obtained in about 89% yield by the addition of benzalazine to boiling 95–98% hydrazine hydrate [10]. We used the same method to synthesize benzisobutyralazine, which likewise has not been described previously.

Both of the mixed azines were yellowish liquids, which distilled in vacuum with very slight decomposition. They were unstable substances and decomposed during storage, especially in air, to give two symmetrical azines corresponding to the original aldehydes according to the scheme:

$$2R{-}CH{=}N{-}N{=}CH{-}R_1 \longrightarrow R{-}CH{=}N{-}N{=}CH{-}R + R_1{-}CH{=}N{-}N{=}CH{-}R_1$$

The reason for this rearrangement is the unequal distribution of electron density in the conjugated system $-C{=}N{-}N{=}C-$ of mixed azines. Radicals of different structure (R and R_1) attract electrons to a different extent and this leads to weakening of the N–N bond and, apparently, to its rupture with the formation of the free radicals $R{-}CH{=}N-$ and $R_1{-}CH{=}N-$, from which stable, symmetrical molecules are formed.

EXPERIMENTAL

Benzacetalazine. Benzylidenehydrazine (6.8 g) was dissolved in 20 ml of absolute ether. Over a period of 20 minutes, 2.5 g of acetaldehyde was added dropwise to the solution, cooled in an ice-salt mixture. The ether solution was dried over sodium sulfate for 2 hours. The ether was removed in vacuum. Distillation of the residue yielded 6.5 g of benzacetalazine (78.3%).

B.p. 76–77° at 3 mm; 96–97° at 8 mm, d_4^{20} 0.9964; n_D^{20} 1;5832; MR 49.00 ; Calc. 46.24*; EMR 2.76

Found %: C 74.05, 73.87; H 6.59, 6.78; N 19.50, 19.29. M 145.3, 145.6. $C_9H_{10}N_2$. Calculated %: C 73.94; H 6.88; N 19.18. M 146.0.

Thus, the substance obtained was benzacetalazine. The light-yellow, oily liquid was insoluble in water. It rapidly decomposed when added to water and gave a stable emulsion on shaking. It dissolved readily in alcohol, ether, and benzene.

Benzisobutyralazine. Benzylidenehydrazine (7.2 g) was dissolved in 24 ml of absolute ether. Isobutyraldehyde (4.4 g) was added dropwise to the solution with cooling in an ice-salt mixture. The mixture was kept at room temperature for 0.5 hour and then left overnight over sodium sulfate. The ether was removed in vacuum. Distillation of the residue yielded 7.6 g of benzisobutyralazine (73.1%).

B.p. 98-98.5° at 3 mm; 113–114° at 7 mm; d_4^{20} 0.9554, n_D^{20} 1.5607, MR 58.95; calc. 55.47; EMR 3.48.

Found %: C 76.20, 75.90; H 7.36, 7.38; N 16.35, 16.13. M 178.0, 173.8. $C_{11}H_{14}N_2$. Calculated %: C 75.83; H 8.09; N 16.08. M 174.2.

Benzisobutyralazine was a quite thick, light-yellow, oily liquid, which was insoluble in water; it decomposed to give an emulsion with water, but dissolved readily in alcohol, ether, and benzene.

Action of hydrazine hydrate on a mixture of benzaldehyde and acetaldehyde. Over a period of 15 minutes, 12.0 g of 80% hydrazine hydrate was added dropwise to a mixture of 6.6 g of acetaldehyde and 16.1 g of benzaldehyde in a bottle with cooling and shaking. The mixture was stirred for a further 20 minutes and left overnight. We isolated 14.3 g (90.5%) (after recrystallization from methyl alcohol) of benzalazine with m.p. 92.5–93° (according to data in [7, 8], m p. 93°). The aqueous layer was saturated with potassium carbonate and the product extracted with ether and dried with sodium sulfate. Distillation yielded 1.5 g (23.8%) of acetalazine.

Decomposition of benzacetalazine. A sample of 30 g of this substance was stored in a distillation flask. After 10 days yellow crystals formed under the liquid layer. When the mixture was heated in a stream of dry air, 2.3 g of acetalazine distilled. After 15 days, a further 1.3 g of the latter was distilled. We isolated a total of 3.6 g (41.9%) of acetalazine. The crystals remaining in the flask were benzaldazine. Recrystallization yielded 18.5 g (86.4%) of this product.

*The refraction of the two nitrogen atoms in azines was taken as 8.277 [11].

Decomposition of benzisobutyralazine. A sample of 7.5 g of this substance was stored in a flask for 20 days. Yellow crystals of benzalazine (4.3 g, 95.8%) were formed and 2.3 g of isobutyralazine (77.0%) was distilled in vacuum.

SUMMARY

1. A method of synthesizing unsymmetrical azines by the action of hydrazine hydrate on a mixture of two aldehydes, which is described in the literatue, was shown to be useless.

2. The mixed (unsymmetrical) aliphatic-aromatic azines benzacetalazine and benzisobutyralazine are described again.

3. These mixed azines are unstable substances, which decompose on storage to two symmetrical azines. This type of rearrangement has not been described in the literature.

LITERATURE CITED

[1] Th. Curtius, Pflug, J. pr. Ch. (2) 44, 192, 535 (1891).

[2] R. Blout, W. Eager and M. Gofstein, J. Am. Chem. Soc. 68, 1983 (1946).

[3] W. H. Perkin, J. Chem. Soc. 127, 1138 (1925).

[4] British Pat. 591275 (1947).

[5] A. N. Kost and I. I. Grandberg, Zhur. Obshchei Khim. 26, 1717 (1956). •

[6] S. A. Tebinov, Zhur. Obshchei Khim. 7, 654 (1937).

[7] K. A. Taipale, Zhur. Russ. Khim. Obshchestv. 63, 243 (1930); Zhur. Obshchei Khim 7, 1383 (1937).

[8] K. Migatake, J. Pharm. Soc. Japan 73, 455 (1953); C. A. 48, 5144g (1954).

[9] H. C. Barany, J. Chem. Soc. 1898 (1949).

[10] Th. Curtius and H. Franzen, Ber. 35, 3234 (1902).

[11] A. N. Kost and I. I. Grandberg, Zhur. Obshchei Khim. 26, 2319 (1956). •

•Original Russian pagination. See C. B. translation.

ISOMERS OF SARCOLYSINE AND THEIR DERIVATIVES

I. SYNTHESIS OF m-DI-(2-CHLOROETHYL)-AMINO-DL-PHENYLALANINE

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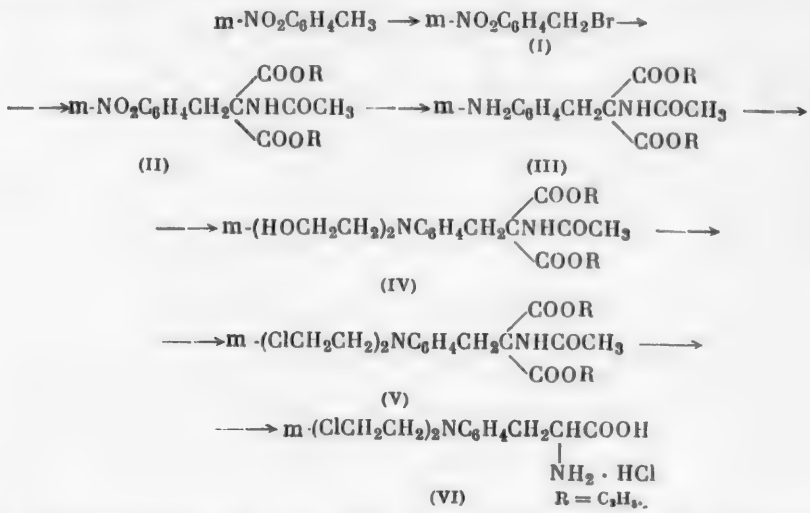
Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4094—4096, December, 1959

Original article submitted June 16, 1958

Some of the most active agents against malignant neoformations are the so-called "alkylating" substances, containing the cytotoxic β-dichlorodiethylamino group. One of the most powerful substances of this type is the hydrochloride of p-di-(2-chloroethyl)-aminophenylalanine ("sarcolysine") [1].

In developing previous investigations, it seemed interesting to us to synthesize the corresponding ortho- and meta-isomers and their derivatives so as to study the action of these substances on tumors in comparison with sarcolysine itself.

In the present article we describe a method of preparing m-di-(2-chloroethyl)-amino-DL-phenylalanine hydrochloride ("meta-sarcolysine"). The synthesis was carried out according to the scheme given below:



We prepared m-nitrobenzyl bromide by the action of N-bromosuccinimide on m-nitrotoluene in CCl_4 in the presence of freshly prepared benzoyl peroxide [2]. Condensation of acetylaminomalonic ester with m-nitrobenzyl bromide yielded m-nitrobenzylacetylaminomalonic ester (II), which was hydrogenated over Raney nickel to m-aminobenzylacetylaminomalonic ester (III). Treatment of the latter with ethylene oxide in dilute acetic acid at room temperature gave m-di(2-hydroxyethyl)-aminobenzylacetylaminomalonic ester (IV). m-Di-(2-chloroethyl)-aminobenzylacetylaminomalonic ester (V) was obtained by reaction of (IV) with thionyl chloride. This reaction was accompanied by considerable tar formation. The best results were obtained by the slow addition of thionyl chloride to (IV) in $CHCl_3$ with cooling and subsequent boiling for 20 minutes.

m-Di-(2-chloroethyl)-amino-DL-phenylalanine hydrochloride (VI) was obtained by hydrolysis of (V) by boiling with concentrated HCl. After recrystallization from 50% alcohol, meta-sarcolysine had m.p. 174–177° (decomp.) with a heating rate of 4° per minute.

Preliminary investigations showed that meta-sarcolysine has a considerable antitumor activity with respect to sarcoma 45.

EXPERIMENTAL

m-Nitrobenzyl bromide (I). Into a 100-ml flask, fitted with a reflux condenser with a calcium chloride tube, were placed 19.0 g of m-nitrotoluene, 20 g of freshly recrystallized N-bromosuccinimide, 0.1 g of freshly prepared benzoyl peroxide, and 50 ml of CCl_4. After being heated on a water bath for 4 hours, the reaction mixture was cooled to room temperature and filtered free from the succinimide formed. The solvent was evaporated from the filtrate and the residue vacuum distilled. We obtained 19.0 g (78% on the bromosuccinimide) of m-nitrobenzyl bromide with b.p. 120–125° at 2 mm and m.p. 48–50°. One recrystallization from ligroin yielded crystals with m.p. 56-57° (according to data in [3]: 58–59°).

m-Nitrobenzylacetylaminomalonic ester (II). With vigorous stirring, 9.3 g of acetylaminomalonic ester was added to a warm solution of sodium ethylate (60 ml of anhydrous alcohol and 0.98 g of sodium). After 10-minutes stirring, a solution of 9.2 g of m-nitrobenzyl bromide in 25 ml of dry benzene was gradually added to the mixture dropwise. When all the benzene solution had been added, the mixture was stirred for a further 4 hours and left in a refrigerator for 12 hours. The precipitate was collected and washed with benzene, alcohol, and water. After being dried, the substance weighed 10.3 g and had m.p. 156.5–157.5°. A further 1.4 g of substance with m.p. 156–157.5° was obtained from the filtrate. The two portions were combined and recrystallized from benzene. We isolated 10.2 g (68.4%) of m-nitrobenzylacetylaminomalonic ester with m.p. 157–158°.

Found %: C 54.2; H 5.6; N 8.1. $C_{16}H_{20}O_7N_2$. Calculated %: C 54.5; H 5.7; N 7.9.*

m-Aminobenzylacetylaminomalonic ester (III). A solution of 3.52 g of (II) in 50 ml of 96% alcohol was shaken with hydrogen in the presence of 1.5 g of Raney nickel for 1.5 hours at atmospheric pressure and 45–50°. Removal of the catalyst and solvent yielded 3.0 g (93.7%) of substance with m.p. 160–162.5°. Recrystallization from alcohol yielded 2.8 g of m-aminobenzylacetylaminomalonic ester with m.p. 162–163°.

Found %: C 59.8; H 6.8; N 8.9. $C_{16}H_{22}O_5N_2$. Calculated %: C 59.6; H 6.8; N 8.7.

m-Di-(2-hydroxyethyl)-aminobenzylacetylaminomalonic ester (IV). To a cooled solution of 1.92 g of (III) in 20 ml of 25% acetic acid was added 3 ml of cold, distilled ethylene oxide and the mixture left at room temperature for 17–20 hours. Neutralization of the solution with sodium carbonate (to pH 7 according to a universal indicator) liberated an oil, which was extracted with ethyl acetate. After drying over anhydrous Na_2SO_4 and removal of the solvent, the residue of m-di-(2-hydroxyethyl)-aminobenzylacetylaminomalonic ester was washed with ether and dried. The yield was 2 g (83.4%) and the m.p. 79–82°. After recrystallization from benzene, the substance had m.p. 84–86°.

Found %: C 58.6; H 7.6; N 6.9. $C_{20}H_{30}O_7N_2$. Calculated %: C 58.5; H 7.4; N 6.8.

m-Di-(2-chloroethyl)-aminobenzylacetylaminomalonic ester (V). A cooled solution of 3.6 ml of $SOCl_2$, distilled twice over wax, in 50 ml of $CHCl_3$ was added dropwise to 2.4 g of (IV) in 150 ml of dry $CHCl_3$. Twenty-minutes boiling and removal of the solvent in vacuum (temperature no higher than 40°) yielded a solid residue weighing 3.7 g. Recrystallization from 80% alcohol ielded 1.7 g (65.4%) of m-di-(2-chloroethyl)-aminobenzylacetylaminomalonic ester with m.p. 84.5–86°. The analytically pure substance had m.p. 86–87°

Found %: C 53.3; H 6.4; N 6.5; Cl 15.7. $C_{20}H_{28}O_5N_2Cl_2$. Calculated %: C 53.6; H 6.3; N 6.3; Cl 15.8.

m-Di-(2-chloroethyl)-amino-DL-phenylalanine hydrochloride (meta-sarcolysine) (VI). A solution of 1.7 g of (V) in 50 ml of 20% HCl was boiled for 6 hours. After treatment with activated charcoal and filtration, the solution was evaporated in vacuum at a temperature not exceeding 40°. The residue (1.7 g) was ground with 50%

*All analyses were carried out in the Analytical Chemistry Laboratory of our institute.

alcohol and recrystallized twice from the same solvent. The meta-sarcolysine thus obtained had m.p. 174–177° with a heating rate of 4° per minute (decomp.). The substance was readily soluble in water and alcohol, but insoluble in ether.

Found %: C 45.5; H 6.0; N 8.2. $C_{14}H_{19}O_2N_2Cl_3$. Calculated %: C 45.7; H 5.6; N 8.2.

SUMMARY

Via m-nitrobenzyl bromide, we synthesized m-nitrobenzylacetylaminomalonic ester, m-aminobenzylacetylaminomalonic ester, m-di-(2-hydroxyethyl)-aminobenzylacetylaminomalonic ester, m-di-(2-chloroethyl)-aminobenzylacetylaminomalonic ester, and m-di-(2-chloroethyl)-amino-DL-phenylalanine hydrochloride (meta-sarcolysine) from m-nitrotoluene.

LITERATURE CITED

[1] L. F. Larionov, A. S. Khokhlov, E. N. Shkodinskaya, O. S. Vasina, V. I. Trusheikina and M. N. Novikova, Byull. Éksp. Biologii i Meditsiny 39, 1, 48 (1955); Author's certificate 104781 (1954).

[2] H. Schmid and P. Karrer, Helv. Chim. Acta 29, 573 (1946).

[3] Norris, Watt and Thomas, J. Am. Chem. Soc. 38, 1077 (1916).

LETTERS TO THE EDITOR

ADDITION OF PHOSPHORUS PENTACHLORIDE TO VINYLETHYLACETYLENE

A. A. Petrov, Yu. I. Porfir'eva and V. I. Savchenko

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Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4096–4097, December, 1959

Original article submitted July 16, 1959

It was previously shown that the addition of phosphorus pentachloride to vinyl- and isopropenylacetylenes proceeds with replacement of one of the hydrogen atoms by chlorine [1]. Treatment of the adducts obtained with SO_2 formed not the expected acid chlorides of chloroalkadienylphosphinic acids (I), which were previously obtained by another method [2], but 1,3-diene acid chlorides with the formula $C_nH_{2n}Cl_2POCl_2$.

It seemed interesting to determine the course of the reaction of PCl_5 with vinylalkylacetylenes, which differ from the previously used vinylacetylenes in the lack of a terminal acetylene grouping.

Experiments showed that vinylethylacetylene added PCl_5 without replacement of hydrogen atoms by chlorine and formed, after treatment of the adduct with SO_2, the 1,3,-diene acid chloride (II) in about 30% yield.

$CH_2{=}CR{-}CCl{=}CH{-}POCl_2$ (I)

$C_2H_5{-}C(POCl_2){=}CCl{-}CH{=}CH_2$ (II)

B.p. 132–133° (3 mm), d_4^{20} 1.3374, n_D^{20} 1.5560.

Found %: P 13.31, 13.24; Cl 46.21, 45.86. $C_6H_8OPCl_3$. Calculated %: P 13.27; Cl 45.56.

We simultaneously obtained a small number of low-boiling products, some of which contained and others did not contain phosphorus.

On hydrolysis, acid chloride (II) gave a crystalline acid with m.p. 123° (from water + HCl).

Found %: P 16.02. $C_6H_{10}O_3PCl$. Calculated %: P 15.76.

The aniline salt of the acid melted at 166° (from acetone).

Found %: N 5.18; P 10.89. $C_{12}H_{17}O_3NPCl$. Calculated %: N 4.83; P 10.69.

The infrared spectrum of the acid chloride (II) had characteristic bands of a chlorine-substituted conjugated system of double bonds (1575 and 1624 cm^{-1}) and of a vinyl group (936 and 986 cm^{-1}). The spectrum contained no frequencies of an allene system (1,4 addition). The substance may have contained a trace of the acetylene acid chloride (3,4 addition) as the infrared spectrum showed a weak band with a frequency of 2213 cm^{-1}. The intense band in the spectrum at 1264 cm^{-1} corresponded to the P=O bond.

LITERATURE CITED

[1] B. A. Vovsi, Yu. A. Sharanin, A. A. Petrov, L. K. Maslii and T. V. Yakovleva, NDVSh, 335 (1958).

[2] Yu. M. Zinov'ev, L. I. Muler and L. Z. Soborovskii, Zhur. Obshchei Khim 24, 380 (1954). *

*Original Russian pagination. See C. B. translation.

NEW METHOD OF PREPARING RADIOACTIVE STANDARDS FOR C^{14}

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Translated from Zhurnal Obshchei Khimii Vol. 29, No. 12, pp. 4097–4099, December, 1959

Original article submitted November 20, 1958

Radioactive standards for determining the absolute activity of preparations containing C^{14} consist either of particles of an insoluble salt (for example, $BaC^{14}CO_3$), included in an organic film, or of thin plates of polymers obtained by polymerization of monomers labeled with C^{14}. The first type of standard is obtained very readily but has shortcomings such as inhomogeneity and ready degradation. Methyl methacrylate, styrene [1], and ethylene [2] have been used for preparing standards of the second type. The standards obtained are homogeneous through the volume and, in particular, on the surface but their preparation involves many operations (synthesis of labeled monomer, polymerization, and treatment of polymer) with relatively large amounts of radioactive material.

The method proposed is based on the preparation of graft copolymers by means of ionizing radiation.

When monomer A is absorbed by a film of polymer B_p and this system treated with ionizing radiation, active centers arising in the chains of polymer B_p will initiate the growth of chains of polymer A_p "grafted" to the skeleton of the polymer. The use of a monomer labeled with C^{14} yields graft copolymers which may serve as radioactive standards. This method makes it possible to eliminate the laborious operations of polymerization and processing of the radioactive polymers.

The standard has strictly constant form and the dimensions of the grafted film remain constant; the growth due to grafting is homotetic and cannot be determined gravimetrically and hence the size of the surface does not change. The carrier used may be a plastic film of various thickness and with the best mechanical properties. Various labeled monomers may be used for grafting and the choice depends on the convenience of synthesis. A suitable choice of skeletal polymer and monomer yields surface-grafted copolymers, which contain no radioactive material within the film. Radiation doses required for grafting are small and do not affect the structure of the skeletal polymer.

Materials. As skeletal polymers we tested polyethylene, polyethylene terephthalate, and polycaprolactam films, and also thin plates of unsaturated polyesters. With the exception of the latter, the polymer films were less than 0.04 mm thick and were infinitely thin to the soft β-radiation of C^{14} so that self-absorption corrections were not required.

The labeled monomers used were ω-styrene-C^{14} and methyl methacrylate-1-C^{14}, but acrylonitrile, vinyl acetate, ethylene etc. could also be used.

Radiation sources. Irradiation was carried out both with Co^{60} γ-radiation and x-rays.

Preparation of standards. The polymer films were washed and dried in vacuum at 50° and then cut to given dimensions with a cutting punch. The film was introduced into the labeled monomer, containing inhibitor, and left for a few minutes for impregnation; the time depended on the concentration of radioactive material in the monomer and the activity desired. The film was then removed, washed free from adsorbed monomer by successive immersion in 3 vessels with solvent for 20–30 seconds in each, and sealed in a glass ampoule in an inert atmosphere.

TABLE

Irradiation time (in hr)	Activity (in counts/min)		
	sample 1: absolute activity $1.3 \cdot 10^{-3}$ μC	sample 2: absolute activity $1.0 \cdot 10^{-2}$ μC	sample 3: unirradiated film
0.5	156	138	180
2	154	136	103
10	156	137	54
60	155	138	—
120	155	138	—
400	156	139	—
1200	155	138	—

The ampoule was irradiated with a dose of approximately $0.75 \cdot 10^6$ rad and opened in a fume hood. The grafted film was extracted, washed with a suitable solvent and dried in vacuum.

Results. The data presented in the table correspond to the following working conditions: a polyethylene terephthalate film, 0.03 mm thick and 2 cm^2 in area, was soaked for 15 minutes in a solution of ω-styrene-C^{14} in styrene (activity 2800 counts/min). It was washed with heptane as described above. The film was irradiated under nitrogen with a dose of $0.75 \cdot 10^6$ rad. The Co^{60} source had a nominal activity of 46 g-equiv of Ra. The measurements were made under an end-window Geiger-Muller counter with a thin mica window of 2.7 mg/cm^2. For testing the constancy of the activity, the film was stored at a pressure of 10 mm Hg at room temperature; after 6 weeks the grafted films had exactly the same activity.

LITERATURE CITED

[1] J. Bevington, G. Guzman and H. Melville, Pr. Roy. Soc. A 221, 453 (1954).

[2] F. Danusso, G. Pajaro and D. Sianesi, J. Polymer. Sci. 22, 179 (1956).

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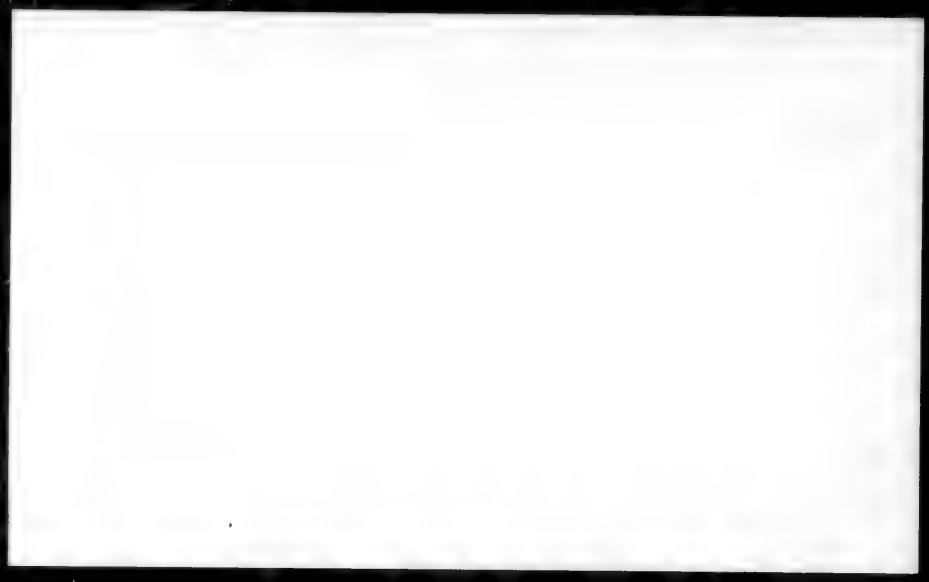
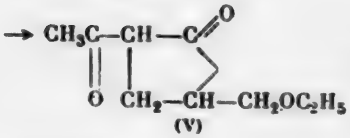
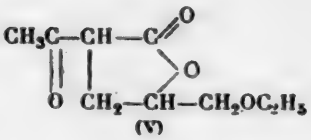


ERRATA

Volume 29, 1959

Number 1

Page	Line	Reads	Should Read
179	10 from bottom	$C_{10}H_{20}O_2$	$C_{10}H_{20}ON_2$
239	21	$C_3H_5O_2PCl_3$	$C_3H_5O_2PCl_3$
316	21	$C_{11}O_{13}O_3S_3Na$	$C_{11}H_{13}O_3S_3Na$
318	compound (V)	 (V)	 (V)

Number 2

361	3	trisubstituted	hexasubstituted
476	5 from bottom	$C_{14}O_{30}ON_2$	$C_{14}H_{30}ON_2$
529	4	$C_8H_8N_2S_2$	$C_8H_8O_2N_2S_2$

Number 3

758	last	$C_{11}H_{18}O_6$	$C_{11}H_{18}O_4$
785	5	$C_{11}H_{14}O_2$	$C_{11}H_{14}O_6$
876	6th formula	$C_{14}H_{21}O_3NS$	$C_{14}H_{21}O_3N_3S$

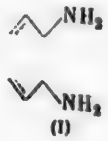
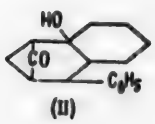
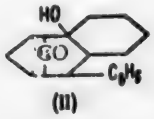
Number 4

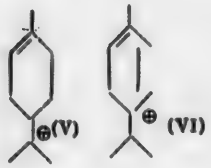
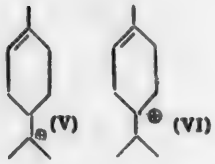
1081	compound (X)	. . . $Si(CH_3)_2$	. . . $Si(CH_3)_3$
1190	compound 9	. . $\equiv(OC_2H_5)_2$	. . $\equiv(OCH_3)_2$
1309	last	$C_{17}H_{18}O_4H_4Cl_2$	$C_{17}H_{18}O_4N_4Cl$

Number 5

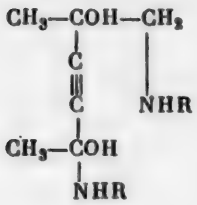
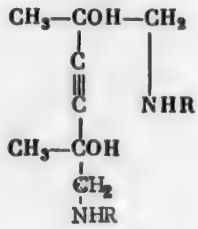
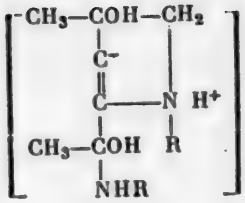
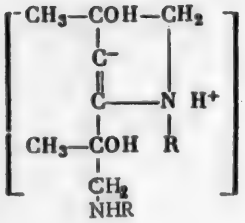
1494	10 from bottom	$C_8H_{16}O_4$	$C_8H_{16}O_4Si$

Number 6

1787	compound IV	$C_{21}H_{25}O_5NP_2$	$C_{21}H_{25}O_4NP_2$
1791	last 2	γ-isothiocyanopropyl-phosphinic acid	γ-isothiocyanopropyl-phosphonic acid
1856	compound (I)	 (I)	(I)
1879	compound (II)	 (II)	 (II)

Page	Line	Reads	Should Read
2046	Table 2, compound 2	$C_6H_4(NO_2)N(NO)CH$	$C_6H_4(NO_2)N(NO)CH_3$
2066	compounds (V), (VI)		

Number 7

2099	compound		
2099	compound		
2154	23	$C_{14}H_{12}NPSCl$	$C_{14}H_{12}N_2SPCl_3$
2155	2 from bottom	$C_{10}H_{14}ONPS_3$	$C_{10}H_{24}ONPS_3$
2168	5 from bottom	C_8H_8Cl	C_8H_9Cl
2272	compound (Ve)	C_6H_6CH-CH	$C_6H_6CH=CH$
2281	6 from bottom	$C_{25}H_{12}O$	$C_{25}H_{42}O$
2284	in Fig. 1	mμ	μ
2311	last	-CH=CH- in the glycol group	hydrogen in the -CH=CH- group
2316	8	photoelectrospectro-photometer	spectrophotometer
2398	13	$C_{18}H_{27}O_5 \cdot HClO_4$	$C_{18}H_{27}O_5N \cdot HClO_4$
2402	4 from bottom	$C_{15}H_{24}O_2N_2K$	$C_{15}H_{23}O_2N_2K$
2403	7 from bottom	$C_{15}H_{24}O_3N_2K$	$C_{15}H_{23}O_3N_2K$

SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.

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